2018 annual report of the European Liver Transplant Registry (ELTR) - 50-year evolution of liver transplantation

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[1]René Adam, [1]Vincent Karam, [1]Valérie Cailliez, [2]John G. O Grady, [3]Darius Mirza, [1]Daniel Cherqui, [4]Jurgen Klempnauer, [5]Mauro Salizzoni, [6]Johann Pratschke, [7]Neville Jamieson, [8]Ernest Hidalgo, [9]Andreas Paul, [10]Rafael Lopez Andujar, [11]Jan Lerut, [12]Lutz Fisher, [13]Karim Boudjema, [14]Constantino Fondevila, [15]Olivier Soubrane, [16]Philippe Bachellier, [17]Antonio D. Pinna, [18]Gabriela Berlakovich, [19]William Bennet, [20]Massimo Pinzani, , [21]Peter Schemmer, [22]Krzysztof Zieniewicz , [23]Carlos Jimenez Romero, [24]Paolo De Simone, [25]Bo-Goran Ericzon, [26]Stefan Schneeberger, [27]Stephen J. Wigmore, [28]Joan Fabregat Prous, [29]Michele Colledan, [30]Robert J. Porte, [31]Sezai Yilmaz, [32]Daniel Azoulay, [33]Jacques Pirenne, [34]Pal-Dag Line, [35]Pavel Trunecka, [36]Francis Navarro, [37]Andres Valdivieso Lopez, [38]Luciano De Carlis, [39]Sebastian Rufian Pena, [40]Eberhard Kochs, [32]Christophe Duvoux and all the other 126 contributing centers (www.eltr.org) and the European Liver and Intestine Transplant Association (ELITA).

1) Paul Brousse Hospital, Univ Paris-Sud, Inserm U935, Villejuif, France
2) King's College Hospital Hospital, London, UK
3) The Queen Elizabeth Hospital, Birmingham, UK
4) Medizinische Hochschule Hannover, Hannover, Germany
5) Centro de Trapianti di Fegato, Torino, Italy
6) Charité- Campus - Virchow klinikum, Berlin, Germany
7) Addenbrooke's Hospital, Cambridge, UK8) St Jame's & Seacroft University Hospital, Leeds, UK
9) C. U. K. GHs Essen, Essen, Germany
10) Hospital Universitario LA FE, Valencia, Spain
11) Cliniques Universitaires Saint Luc, Brussels, Belgium
12) Universitatsklinikum Hamburg Eppendorf, Hamburg, Germany
13) C.H.U. Rennes, Hopital De Pontchaillou, Rennes, France14) Hospital Clinic I Provincial de Barcelona, Barcelona, Spain
15) Hopital Beaujon, Clichy, France

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16) C.H.R.U. De Strasbourg, Strasbourg, France
17) University Of Bologna, Bologna, Italy
18) Klinishe Abteilung Fur Transplantation, Wien, Austria19) Sahlgrenska University Hospital, Gothenborg, Sweden
20) Royal Free Hospital, London, UK.
21) Universitatsklinikum Heidelberg, Heidelberg, Germany
22) Medical University Of Warsaw Banacha, Warsaw, Poland
23) Hospital 12 De Octubre, Madrid, Spain
24) Ospedale Cisanello, Pisa, Italy
25) Huddinge Hospital, Huddinge, Sweden
26) University Hospital, Innsbruck, Austria
27) University Of Edinburgh Royal Infirmary, Edinburgh, UK
28) Hospital Universitari De Bellvitge, Barcelona, Spain
29) Papa Giovanni 23 Hospital, Bergamo, Italy
30) University Medical Center Groningen, Groningen, The Netherlands
31) Inonu Universitesi, Malatya, Turkey
32) Hôpital Heri Mondor, Créteil, France
33) Universitaire Ziekenhuizen Leuven, Leuven, Belgium
34) Rikshospitalet, Oslo, Norway
35) Transplancenter Ikem, Prague, Czech Republic
36) Hopital Saint Eloi, Montpellier, France
37) Hospital De Cruces, Baracaldo Vizcaya, Spain
38) Ospedale Niguarda Ca Granda, Milano, Italy
39) Hospital Universitario Reina Sofia, Cordoba, Spain
40) Chirurgische Klinik Und Poliklinik Klinikum rechts Der Isar, Munchen, Germany
The order of the sixteen co-authors was determined according to the decreasing number of liver transplants recorded in the ELTR
The list with all the centers is available at the following link:
http://www.eltr.org/spip.php?page=centers-tous

Corresponding author:

René Adam, MD, PhD.
Centre Hépatobiliaire, Hôpital Paul Brousse
12-14, Av Paul-Vaillant-Couturier
B.P. 200, F-94804 Villejuif Cedex, France.
Tel: +33 1 45 59 32 88
Fax: +33 1 45 59 38 57
E-mail: rene.adam@aphp.fr

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List of abbreviations:

ELTR	European Liver Transplant Registry
ELITA	European Liver and Intestine Transplant Association
ESOT	European Society of Organ Transplantation
LT	liver transplantation
HCV	Hepatitis C virus
HBV	Hepatitis B virus
ALD	Alcoholic liver disease
Retx	Retransplantation

ABSTRACT

The purpose of this registry study was to provide an overview of trends and results of liver transplantation in Europe from 1968 to 2016.

This data on liver transplantation (LT) was collected prospectively from 169 centers from 32 countries, in the European Liver Transplant Registry (ELTR) beginning in 1968. This overview provides epidemiological data, as well as information on evolution of techniques, and outcomes in liver transplantation in Europe over more than 5 decades; something that cannot be obtained from only a single center experience.

INTRODUCTION

Background of the European Liver Transplant Registry

Created in 1986, the ELTR has collected the data of liver transplantation (LT) from 175 centers all over Europe since 1968. The registered data represents more than 95% of the overall European data compared to the published official figures [1].

Questionnaire

The ELTR questionnaire includes data on indications for LT, donors and recipients characteristics, technical aspects of LT (with reduced, split, domino, live and non-heart beating donors), initial and current regimen of immunosuppression, patient outcomes, and cause of death or graft failure. The ELTR has developed an online application (Electronic Data Capture – EDC) for collecting data. A Web-based module was developed to allow for real-time data capture. Software, questionnaires, validation routines and statistics are located on a central server, which can be accessed by the participating centers with a standard internet browser [2].

To avoid an overlap in case of multiple diagnoses, the ELTR has two variables to report the diagnosis (Disease1 & Disease2) and an open field for specification in case a diagnosis is not available in the official pull-down menu, or in case there are more than two combined diagnoses. A standard procedure was stated accordingly for the data entry and their analysis in each condition.

Quality control of the data

The data-entry process is dynamically controlled. The data are subjected to routine checks for completeness, consistency, and range. Comprehensive logical intra- and inter-updates are performed. In addition, a control of the good adequacy between ELTR questionnaire and patient charts is performed by randomly conducted audit visits to the centers. The ELTR audit visits have been continuously conducted since 1998 with, initially 10 randomly selected centers per year up to the year 1999, and 5 centers per year since 2000. Two auditors perform the visit with the condition that both are not from the visited country. Ten percent of center's files, with a minimum of 20 and a maximum of 50, are analyzed to check data for completeness and consistency. The audit visits serve also to train staff members, and to

introduce amendments in the procedure. It is also the opportunity to meet with the staff of centers, something that is valuable for creating a team spirit. The ELTR is considered as the pioneer of external audit visits of a scientific registry. The audit report is sent confidentially to the head of the center with all the discrepancies noted, and the recommendations necessary to improve the data entry included. The results of all center audits are presented during the ELTR biennial workshops, where all the contributing centers are invited. A recent analysis of the ELTR audit data (38 centers from 16 countries, 57,575 variables from 1458 patient files, from 2010 to 2016) showed that the overall rates of completeness and consistency were 94.5% and 97.3%, respectively. Audit visits are an indicator of the quality of data, and represent one of the pillars of the ELTR. These results have indicated that ELTR data are reliable, and the scientific results of ELTR can be considered credible and representative of LT in Europe [3-6].

Partnership with Organ Sharing Organizations (OSOs)

The ELTR has established agreements with the main national and international OSOs: United Kingdom Transplant Service Support Authority – UK NHS Blood and Transplant, Spanish Organizacion Nacional de Trasplantes - ONT, Scandinavian Scandiatransplant - SKT, Dutch Transplant Foundation - NTS, Eurotransplant Foundation - ET, French Agence de la Biomédecine – ABM to exchange data collected from European Centers and to cross check common data between OSO and ELTR.

Source of the data

There are two sources of ELTR data; 72% of data (63% of centers) are shared with the OSOs and 28% of data (37% of centers) are directly entered into the ELTR EDC platform. Some variables were added to the questionnaire, and some definitions have changed since the registry was created in 1986. To adapt the ELTR to these evolutions, an experts committee

was appointed to oversee the standardization of the questionnaire. The ELITA (European Liver and Intestine Transplant Association) board and the OSOs share this concern and are also attentive to all the evolutions.

Previous ELTR achievements

The ELTR regularly carries out thematic studies related to the different fields of LT. These studies minimize the potential biases, by assessing interactions between confounding factors and identification of independent predictors among all the ELTR variables that can have an impact on the outcome. A sample of these studies is cited in the references of the manuscript. With reports concerning LT for specific hepatic diseases [7-24], analysis of the impact of the type of preservation solution [25], and of the immunosuppressive regimen on the patient outcome [26], ELTR has helped develop risk models for mortality following liver–transplantation [27, 28]. Owing to the large cohort of patients, the exhaustiveness, and quality of the data, and the long follow up provided by the ELTR, the results are really representative of liver transplantation in Europe.

The objective of this paper is to report these results and their evolution in adults as well as in pediatric recipients.

PATIENTS AND METHODS

The whole data since 1968 was considered initially to show the evolution of results of LT in Europe since its initial development. The rest of analysis was then undertaken considering two different periods: (a) January 1988 to December 2016 (147,161 LT – 127,851 patients) [January 1988 was chosen corresponding to the introduction and widespread use of cyclosporine-based immunosuppression, and standardization of the surgical procedure], (b)

the last 15-yr period data from January 2002 to December 2016 (99,562 LT – 91,183 patients) to give a more recent evaluation of LT results in Europe.

Data were generally analyzed as a whole (except for some variables), without making a distinction between adult and pediatric population, the latter representing 10% of LT in Europe.

Kaplan–Meier analysis was used to estimate graft and patient survival stratified by conditions group; statistical analyzes were performed using the log–rank test ($p<0.05$ as significant) with SAS® Version 9.1.3 Entreprise Guide version 5.1 (Copyright© 2012 by SAS Institute Inc., Cary. NC. USA). The dynamics of data control was continued during the statistical analyzes. Calculation of survival rates was determined by the actuarial method.

RESULTS

From May 1968 to December 2016, the ELTR has collected data concerning 146,782 liver transplantations (LTs) in 132,466 patients, from 169 Centers, and 32 countries (Figure 1). This data gives a comprehensive overview of the status and evolution of LT in Europe. Both the number of transplant centers and the annual number of LT's performed in Europe have gradually increased since the ELTR was created (Figure 2). However, after an exponential increase from the eighties, a plateau seems to have been reached in recent years with about 7,300 LTs performed all over Europe annually

Main indications of LT in Europe

The main indications for LT in Europe with the corresponding graft and patient survival rates at 1, 5, 10 and 15 years in the whole ELTR population and in the last 15 years cohort are listed in Table 1. Twenty-year survival is provided for the whole ELTR population. Cirrhosis was the most frequent indication (50%), mainly related to either viral infection (22% with 12% of hepatitis C virus (HCV) infection and 5% of hepatitis B virus (HBV) infection), or to alcohol abuse (19%). Combined viral and alcoholic (ALD) cirrhosis represented 2.4% of indications, with 2% of HCV-ALD. Cirrhosis is followed by three major indications: primary liver tumors (17%, predominantly hepatocellular carcinoma – HCC, 15%), cholestatic liver diseases (10%), and acute hepatic failure (9.1%, 2% of which are virus-related, 2.4% drug related, 0.3% toxic non-drug related and 4.4% of unknown cause). The most common etiologies of the underlying cirrhosis in HCC patients were HCV (43%), ethanol abuse (27%) and HBV (16%). Cholestatic diseases included primary biliary cirrhosis (5%) and primary sclerosing cholangitis (5%). Biliary atresia (4%) represented the major congenital biliary disease. Metabolic diseases represented 6% of all the indications with three major indications being familial amyloidotic polyneuropathy, Wilson disease, and alpha-1-antitrypsin deficiency (1% each). Budd-Chiari and benign liver tumors (mainly polycystic disease) represented only 1% of the indications for LT. Secondary liver tumors (mainly neuroendocrine) represented 0.5% of LT's.

Indications for Pediatric liver transplants

The proportions of the main indications for LT are differently distributed according to the age of recipients. While biliary atresia and metabolic diseases were the major indications in pediatric patients (≤18 years), cirrhosis with end stage liver disease, and cancer were the

major indications in adults. An exponential increase in the proportion of cancer cases was noted with recipient age. Acute liver failure (ALF) mostly of unknown cause was frequent in young patients, with the highest incidence at 18-24 years.

Evolution of indications

The percentage of main indications has significantly changed with time (Figure 3). Whereas cancers represented 12% of indications before 1997, their incidence has doubled in the last decade to represent currently more than 24%. Metabolic diseases and primary sclerosing cholangitis have slightly increased during the last decade. Conversely, while comparing the last decade with the previous one, we found that the proportion of cirrhosis alone, ALF and primary biliary cholangitis decreased. The decrease in cirrhosis is mainly due to the decrease in HCV cirrhosis, and the reduction of ALF cases is mainly due to the decline of ALF of unknown origin.

Survival according to the indication for LT

When all indications were considered, during the entire study period, patient survival rates were 83% at 1 year, 71% at 5 years, 61% at 10 years, 51% at 15 years, and 41% at 20 years. After an improvement between 1985 and 2000, the survival of patients appears to be relatively steady since 2000 (Figure 4).

The improvement in survival was seen in patients transplanted for all the three main indications; cirrhosis (Figure 5A), fulminant hepatitis (Figure 5 C) but was particularly regular in LT for cancers (Figure 5C). The 5-year patient survival rate was significantly better for cirrhosis (71%) than for primary liver tumors (64%, $p<0.001$) and acute hepatic failure

(65%, p<0.001). HBV and HCV co-infection had a better 5-year survival (80%) compared to mono-infection with HCV (64%) or HBV (74%). The better 5-year survival rates obtained in metabolic diseases (79%), cholestatic disease (79%) and congenital biliary disease (85%), are partly explained by the high percentage of children in these groups. The survival rates in adults and children were respectively, 76% and 85% for metabolic diseases, 79% and 86% for cholestatic disease and 82% and 85% for congenital biliary disease. The details of survival rates at 1, 5 and 10, 15 and 20 years according to the primary indication are listed in Table 1.

Although the 5-year survival improved in the 15 recent years for all the indications, the most important gain in survival was observed in LT for primary liver tumors (67%), liver metastases (61%) and acute liver failure (69%).

Since the adoption of the transplantation Model for End-stage Liver Disease score (MELD) score in the majority of European countries in 2006-2007, the proportion of patients with a high MELD score (>30) at transplant has almost doubled. However, the survival of these patients is less optimal, especially for those with a MELD score at transplant higher than 40 (Figure 6).

Survival according to donor and recipient characteristics

Donor characteristics

The majority of donors were male (57%). Fifty-eight percent were younger than 50 years, whereas 23% were older than 60 years. A gradual increase of the percentage of livers coming from septuagenarian donors was observed (1% in 1993, 10% in 2005 and 20% in 2015) in relation to the increasing gap between a growing waiting list and a relatively stable donor

pool (Figure 7). Graft survival when organs were procured from donors younger than 55 years was significantly better than that with organs from donors older than 65 years (67% vs. 60% at 5 years, p<0.0001) (Figure 8). However, attention should be paid to the donor to recipient matching to interpret these results, older donor livers being more frequently transplanted to older recipients.

Recipient age

In addition to the better 5-year survival of pediatric versus adult LT recipients (90% vs. 81%, p<0.0001), an influence of age was noted for adult recipients. Survival rates were 75% for adults aged 18 to 45 years, 71% for 46-60 years, 65% for 60-70 years, and 60% for septuagenarians. However, average age of transplanted recipients has increased steadily during the last decade, and patients older than 60 years, who represented less than 5% in the 1980s, currently represent more than 30% of transplant recipients (Figure 9). Older grafts are more frequently transplanted to older recipients. Septuagenarian recipients received 43% grafts older than 60-years and only 12% of grafts younger than 30-years, explaining at least in part, the difference in survival between recipient age groups (Figure 10). Importantly, LT offered a 10-year survival up to 40% in septuagenarians.

Blood group compatible and incompatible transplants

In elective conditions, 93% of LTs were isogroup, and 6.5% were compatible, whereas in emergency, 3% of LT were incompatible. In both elective and emergency conditions, isogroup LTs had a better 5-year survival compared to compatible or incompatible LTs (66% vs. 62% vs. 57%, p<0.0001) and (56% vs. 53% vs. 28%, p=0.001), respectively. However, the use of these incompatible grafts in emergency indications allows a 38% survival rate at 1 year in patients otherwise expected to have a fatal outcome.

Survival according to surgical technique

Auxiliary grafts represented 0.5% of overall LTs with a similar graft survival as compared to non-auxiliary grafts in urgent (5-year survival rates: 57% vs. 56%), and elective (66% vs. 69%) indications. The shorter the ischemia time; the better was the graft survival. Five-year survival was 70% for ischemia time <6 hours, 67% for 6-12 hours, 63% for 12-15 hours, and 58% for >15 hours. The use of static graft preservation solutions evolved during three distinct periods: period 1 before 1990 with the main use of Collins solution; period 2 between 1990 and 2000 with the almost exclusive use of UW (University of Wisconsin); period 3 after 2000 with an increasing use of new solutions with different characteristics such as HTK, Celsior, IGL 1 or SCOT (Figure 11). Overall graft survival at 5 years for the main solutions was 74% for Celsior and IGL 1, 72% for UW and 69% for HTK (Figure 12). If only partial livers were considered, survival was 83% for IGL 1, 79% for Celsior, 77% for UW and 71% for HTK.

Alternative procedures to LT using full size livers from donors after brain death (DBD) have been increasingly used in recent years. While representing less than 10% before 2000 they concerned more than 20% of overall LT procedures after 2000 and 75% in pediatrics. A differentiation between adult and pediatric patients is necessary; because alternative techniques are used differently in each population and the patient's outcome may differ.

Adult population

Before 1994, alternative procedures concerned mainly reduced and split livers. Domino grafts were introduced in 1994 and living donation in 1996. Donation after cardiac death (DCD) was introduced in 2001 and since then, has gradually increased to represent currently almost

40% of the alternative procedures in adults. Consequently, the proportion of split, living, reduced and domino grafts has decreased. The latter two modalities are really associated with the more significant decrease (Figure 13A). Ten-year graft survivals for each type of graft are summarized in Figure 13B. Survival at 5 years was similar between DBD full size grafts, split liver, domino and DCD (66% to 67%), but higher than that of reduced grafts and living donors (63% in both).

Pediatric population

Before 1988, alternative procedures concerned mainly reduced livers. Split livers were introduced in 1988 and living donation in 1991 and since their introduction both have gradually increased to represent currently more than 90% of the alternative procedures in children (Figure 14A). Ten-year graft survivals for each type of graft are summarized in Figure 14B. Survival at 5 years was similar between DCD and living donors (80% and 78%, respectively), but higher than that of DBD full size grafts, split liver and reduced grafts (74%, 71% and 65%, respectively). Domino transplant is rarely used in pediatric patients.

Mortality after LT

While 1 year patient survival was 81% between 1995 and 1999, it has dramatically improved to reach 86% after 2010 (Figure 4). The critical period for post-LT outcome is represented by the first year: 46% of deaths and 67% of re-LT occur within the first year after LT (Figure 15). In 44% of cases, re-LT is indicated in the month after primary LT, and more than a half (59%) of patients who die, do so within the 6 months after LT.

Data represented in figure 16 correspond to the distribution of main causes of death according to the time of their incidence. Main causes of death in the 28,637 patients who died after

primary LT or Re-LT were differently distributed. Whereas death from primary graft non-function or dysfunction, infections and technical (biliary or vascular) complications were more frequent within the first 6 months post-LT, tumor or non-tumor recurrence and tumor de novo were more frequent after the first month. Interestingly, the proportion of tumor and non-tumor recurrences as a cause of death is decreasing during the last years.

Re-transplantation

Five-year graft survival rates following a second and a third LTs were 48% and 42% respectively, significantly lower than those for primary LT (66% - P<0.0001) (Figure 17).

Re-LT was indicated in 8,482 cases mainly for primary non-function, technical complications (biliary or vascular) and rejection within the first month post-LT. Tumor or non-tumor recurrences and de novo tumor were more frequent after the first month (Figure 18). Late re-LT, more than 1 month after the first LT, has a significantly better graft survival than early re-LT performed within the month after the first LT (50% vs. 45% at 5 years, p<0.0001) (Figure 19). Re-LT which is mostly used in young patients (Figure 3A) has declined during the last decade (Figure 3B). Interestingly, tumor causes and non-tumor recurrence are decreasing during the last years, whereas technical complications, primary graft non-function or dysfunction and infection are increasing.

Waiting time

When more than 90% of candidates waited less than 3 months in the 80s, they represented 70% in the 90s and slightly more than a half since 2000. This evolution is likely due to three main reasons: the increase of the number of candidates for transplantation following the

advent of more and more effective immunosuppressive treatments, the scarcity of grafts and the use of the MELD which gives priority to the sickest candidates. The 5-year survival of patients who have spent less than 3 months on the waiting list, certainly because they were more severe, was 70%, 5% lower than that of all the other groups of waiting times in the list ($p<0.0001$).

DISCUSSION

The ELTR data provides a descriptive overview of the overall situation of liver transplantation in Europe. There is of course heterogeneity in the policies in the 29 contributing countries. This manuscript summarizes the results as a whole, and represents a kind of freeze-frame rather than a generalized statement for Europe. At the same time, the ELTR remains the unique entity capable of providing such statistics, capable of giving a global snapshot of the European experience, and helping to identify important trends that may guide further practice.

Liver transplantation has become the best, if not the only effective treatment for severe irreversible liver disease. More than 7,000 LTs are performed annually in Europe, and the results look satisfactory at 5 years (71% survival) with still a room for improvement at long-term (61% at 10 years and 41% at 20 years). The demand far exceeds the availability of organs for transplantation. It is therefore essential to continue to promote organ donation in Europe in order to avoid mortality on the waiting list, and a “drastic” selection of candidates. By allowing the transplant of the sickest candidates first, the MELD score has dramatically decreased the risk of death on the waiting list. However, the post-LT survival of high MELD score patients is less optimal, mostly for those with MELD score at transplant higher than 40. It also appears essential to continue to improve the perioperative management of LT at all

levels, along with a better prevention of long-term complications. The data provided by the ELTR are a basis to target the timing, and fields to improve the results.

The main indication for LT is cirrhosis with end stage liver disease. However its proportion is decreasing continuously as compared to HCC. Fulminant hepatitis of unknown cause is also declining. Such relative diminution of cirrhosis is mainly related to the accelerated decline in HCV indications as a result of effective direct-acting antiviral drugs [17]. Thus, hundreds of liver grafts every year are becoming available for indications other than HCV. Even though NASH related cirrhosis is still less frequent in Europe compared to the US, it is anticipated to become the leading indication for liver transplantation within the next decade.

In terms of results, all the indications have shown an improvement of survival especially HCC, mainly due to a better selection of patients, and the increasing effectiveness of down-staging techniques [18]. The ELTR cohort of patients has also established that some rare malignant tumours like hepatic hemangiosarcoma should be considered absolute contraindications for LT [19], while others like hereditary hemorrhagic telangiectasia [8] or hepatic epithelioid hemangio-endothelioma represent a good indication even in the presence of limited extrahepatic disease [12, 24].

The average age of transplanted recipients has increased steadily during the last decade and a third of patients transplanted nowadays are > 60 years. Noteworthy, LT can offer a 10 additional year benefit to 40% of septuagenarians. Also, an increasing number of transplanted liver grafts are coming from older donors with in most cases, the application of the old-to-old rule concerning the donor to recipient matching.

Alternatives to the conventional DBD full size graft are increasingly used in Europe. Split liver and living donation are increasingly used both in adult and pediatric LT, and DCD grafts are mostly used in adults with quite good survival results. Domino and reduced livers seem to

be gradually disappearing. Optimization of donor management and organ preservation, offers the most realistic way to improve both the quality and pool of current organs. While only UW solution was used before 2000, an increasing number of new solutions are available today; the choice in preservation solution may have an independent impact on graft survival [25].

Also, while the introduction of cyclosporine and more recently Tacrolimus optimised immunosuppressive protocols, there is still room for improvement as recently shown by the use of prolonged release tacrolimus [26].

As a cause of graft loss, technical complications, primary graft non-function or dysfunction and infection are increasing, relatively. This could be related to the increasing use of marginal grafts coming from expanded donor criteria. Conversely, de novo tumor and non-tumor recurrence as cause of graft loss or mortality are decreasing during the last years.

There are some limitations to our study. Data quality, reliability and representativeness is an everyday concern for the ELTR since its creation in 1986. With this constantly in mind, the ELTR has implemented several procedures and adapted them all along the years to control the quality of data, from collection, to statistical analysis. However, biases may persist as for all observational studies; therefore, the interpretation of these descriptive data must be done with caution. Lost-to-follow-up (LTFU) patients are a real problem in the reported outcome. It is mainly related to the increasing number of transplanted patients who move to another place within a country or outside the country. More than 72% of ELTR data are shared with official OSOs who have setup a drastic tracking procedure to minimize the rate of LTFU. The remaining 28% who enter the data directly in our platform are regularly invited to consult the dynamically updated list of queries to solve all discrepancies and to report a recent patient follow-up.

By the prospective evaluation of almost all patients transplanted in Europe since the last fifty years, the ELTR provides valuable data concerning the evolution of LT, the dynamic changes in indications, in donor and recipients profile, as well as in preservation, technical aspects and post-transplant management. This data can help refine the indications for transplant in rare diseases, and establish new guidelines, while targeting the real fields which need improvement in order to optimize the results of liver transplantation.

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ACKNOWLEDGMENTS

The authors are indebted all the 174 contributing centers that are listed at the following link http://www.eltr.org/spip.php?page=centers-tous

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LEGENDS

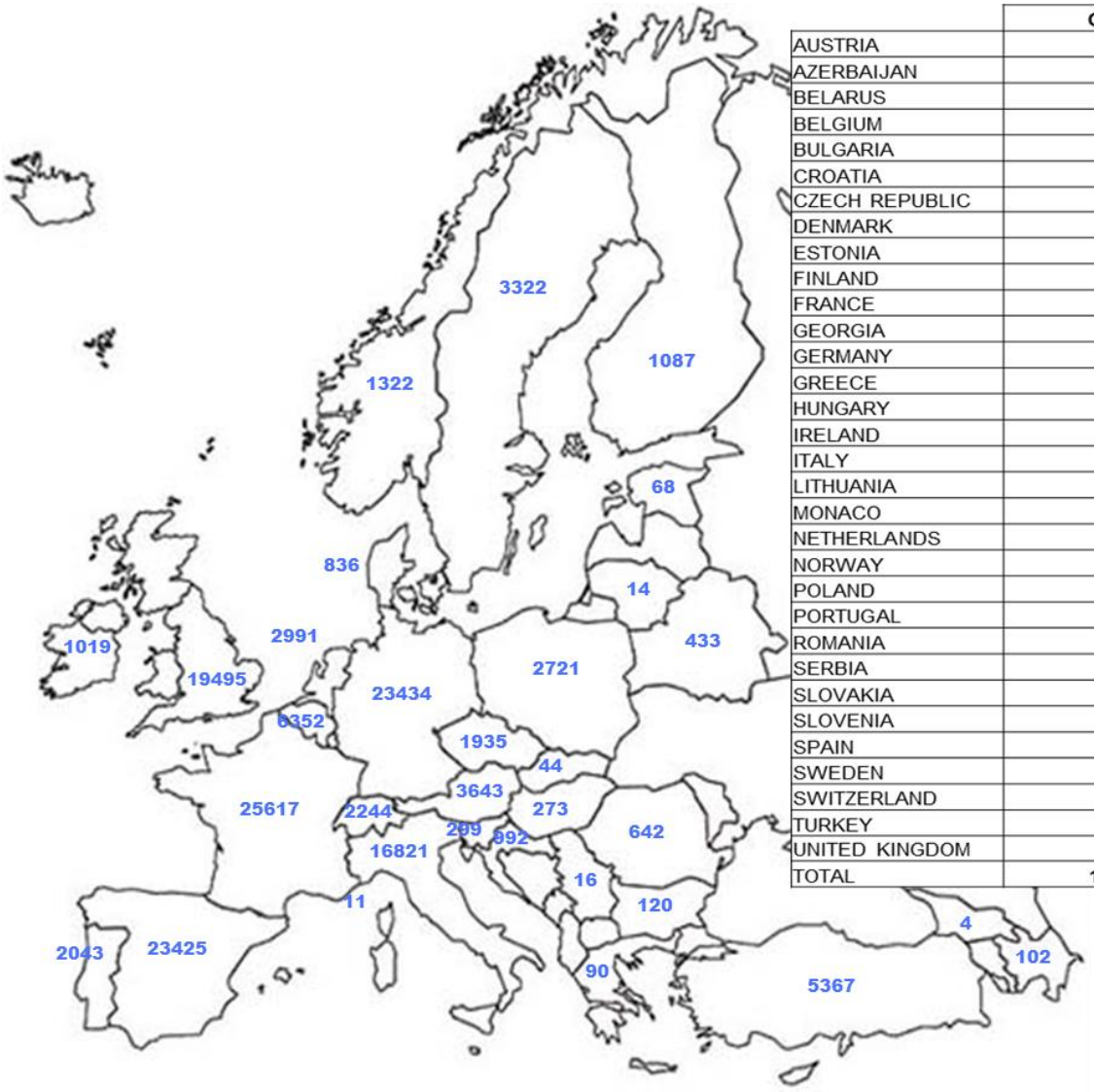
Table 1: Primary indication of LT in Europe and the corresponding graft and patient survival rate.

Figure 1: Number of LTs performed in each country, overall and living related liver transplantation (LRLT)(May 1968 – December 2016).

Figure 2: Evolution of 147,161 LTs performed in Europe since May 1968.

Figure 3: Evolution of indication according to three eras.

The legends of the remaining figures are in the top of each figure.



	Overall	LRLT
AUSTRIA	3643	68
AZERBAIJAN	102	102
BELARUS	433	20
BELGIUM	6352	587
BULGARIA	120	25
CROATIA	992	5
CZECH REPUBLIC	1935	3
DENMARK	836	8
ESTONIA	68	0
FINLAND	1087	0
FRANCE	25617	519
GEORGIA	4	4
GERMANY	23434	1346
GREECE	90	0
HUNGARY	273	0
IRELAND	1019	0
ITALY	16821	267
LITHUANIA	14	0
MONACO	11	0
NETHERLANDS	2991	50
NORWAY	1322	3
POLAND	2721	317
PORTUGAL	2043	26
ROMANIA	642	112
SERBIA	16	1
SLOVAKIA	44	0
SLOVENIA	299	0
SPAIN	23425	401
SWEDEN	3322	80
SWITZERLAND	2244	87
TURKEY	5367	4048
UNITED KINGDOM	19495	342
TOTAL	**146782**	**8421**

Figure 1

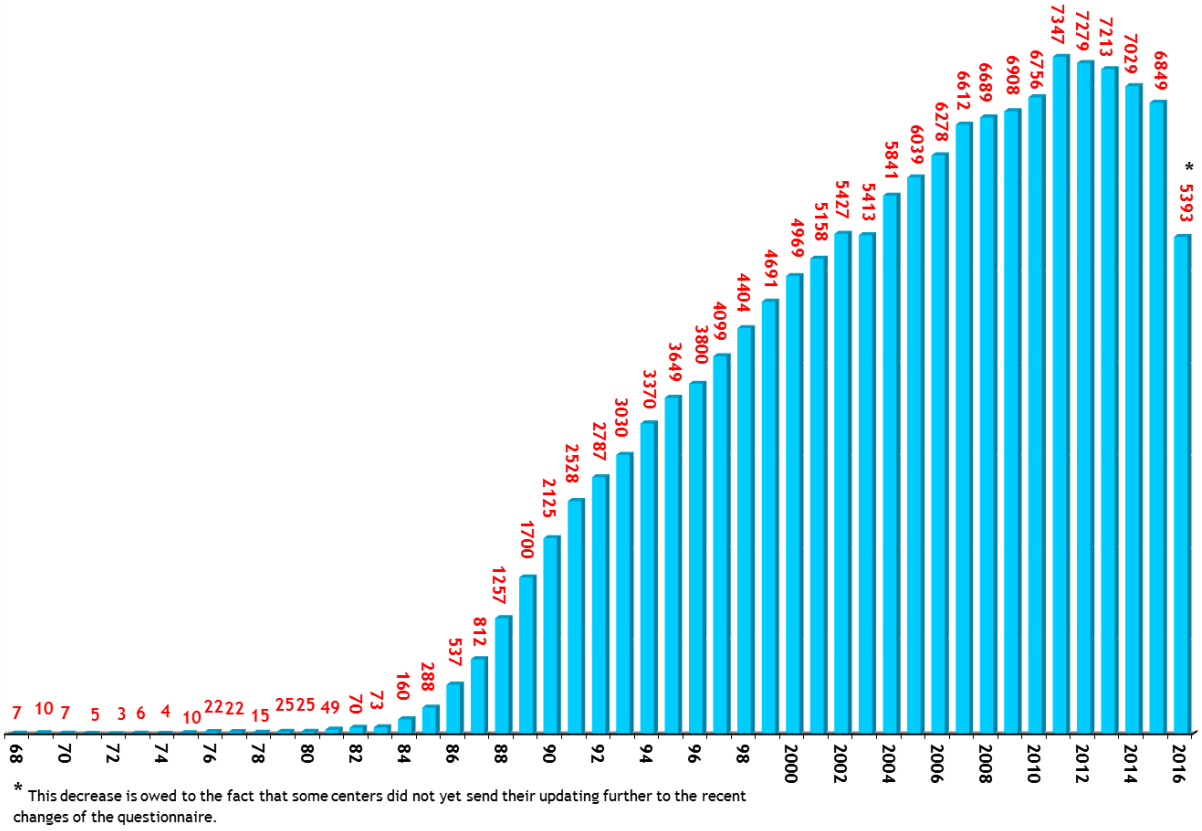


Figure 2

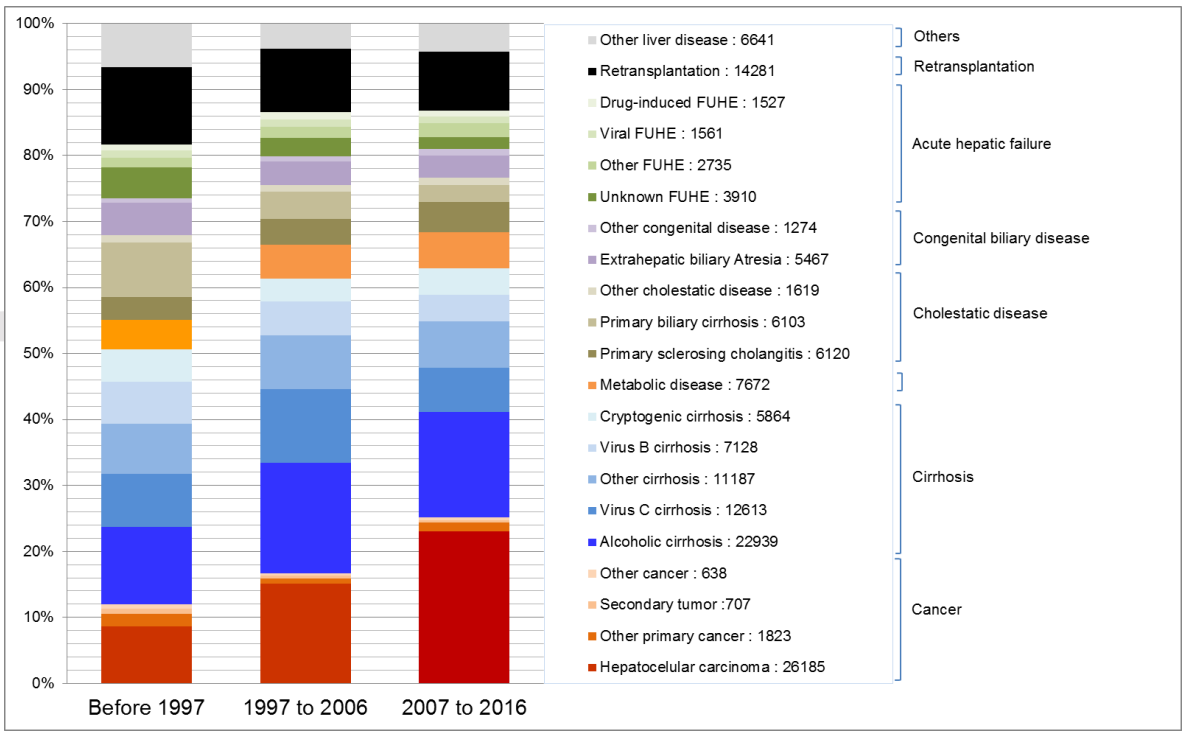
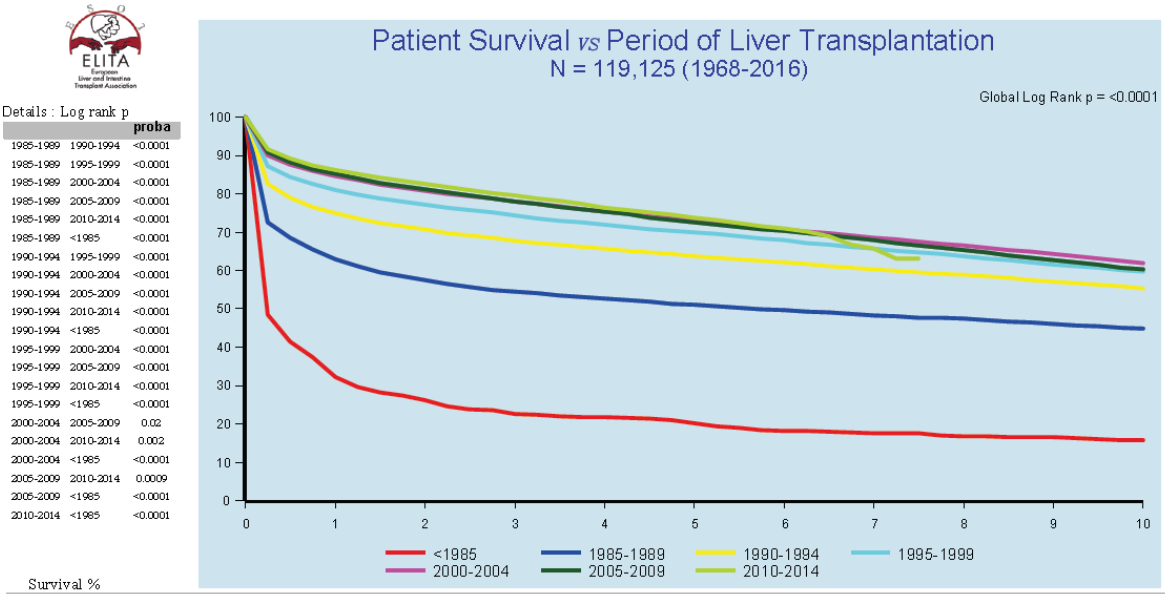


Figure 3



Details : Log rank p

		proba
1985-1989	1990-1994	<0.0001
1985-1989	1995-1999	<0.0001
1985-1989	2000-2004	<0.0001
1985-1989	2005-2009	<0.0001
1985-1989	2010-2014	<0.0001
1985-1989	<1985	<0.0001
1990-1994	1995-1999	<0.0001
1990-1994	2000-2004	<0.0001
1990-1994	2005-2009	<0.0001
1990-1994	2010-2014	<0.0001
1990-1994	<1985	<0.0001
1995-1999	2000-2004	<0.0001
1995-1999	2005-2009	<0.0001
1995-1999	2010-2014	<0.0001
1995-1999	<1985	<0.0001
2000-2004	2005-2009	0.02
2000-2004	2010-2014	0.002
2000-2004	<1985	<0.0001
2005-2009	2010-2014	0.0009
2005-2009	<1985	<0.0001
2010-2014	<1985	<0.0001

Survival %

class of LT1 date	1 yr	2 yrs	3 yrs	4 yrs	5 yrs	6 yrs	7 yrs	8 yrs	9 yrs	10 yrs
1985-1989	63%	57%	54%	53%	51%	50%	48%	47%	46%	45%
1990-1994	75%	71%	68%	66%	64%	62%	60%	59%	57%	55%
1995-1999	81%	77%	74%	72%	70%	68%	66%	64%	62%	60%
2000-2004	85%	81%	78%	75%	73%	71%	69%	66%	64%	62%
2005-2009	85%	81%	78%	75%	73%	70%	68%	65%	63%	60%
2010-2014	86%	83%	79%	76%	74%	71%	66%			
<1985	32%	26%	23%	22%	20%	18%	18%	17%	17%	16%

Number of exposed patients

	Total	1 yr	2 yrs	3 yrs	4 yrs	5 yrs	6 yrs	7 yrs	8 yrs	9 yrs	10 yrs
1985-1989	3967	2464	2250	2132	2056	1990	1929	1861	1817	1749	1687
1990-1994	11914	8806	8272	7901	7603	7332	7092	6822	6546	6241	5885
1995-1999	18156	14384	13591	12955	12327	11722	11021	10342	9743	9121	8620
2000-2004	23773	18963	17420	16272	15294	14421	13645	12832	12016	11215	10292
2005-2009	28813	22636	20468	18755	17480	15977	14319	11412	7851	4776	2592
2010-2014	32030	23232	17687	11871	7277	3891	1189	98	0	0	0
<1985	472	152	124	107	103	95	86	83	78	77	74

Figure 4

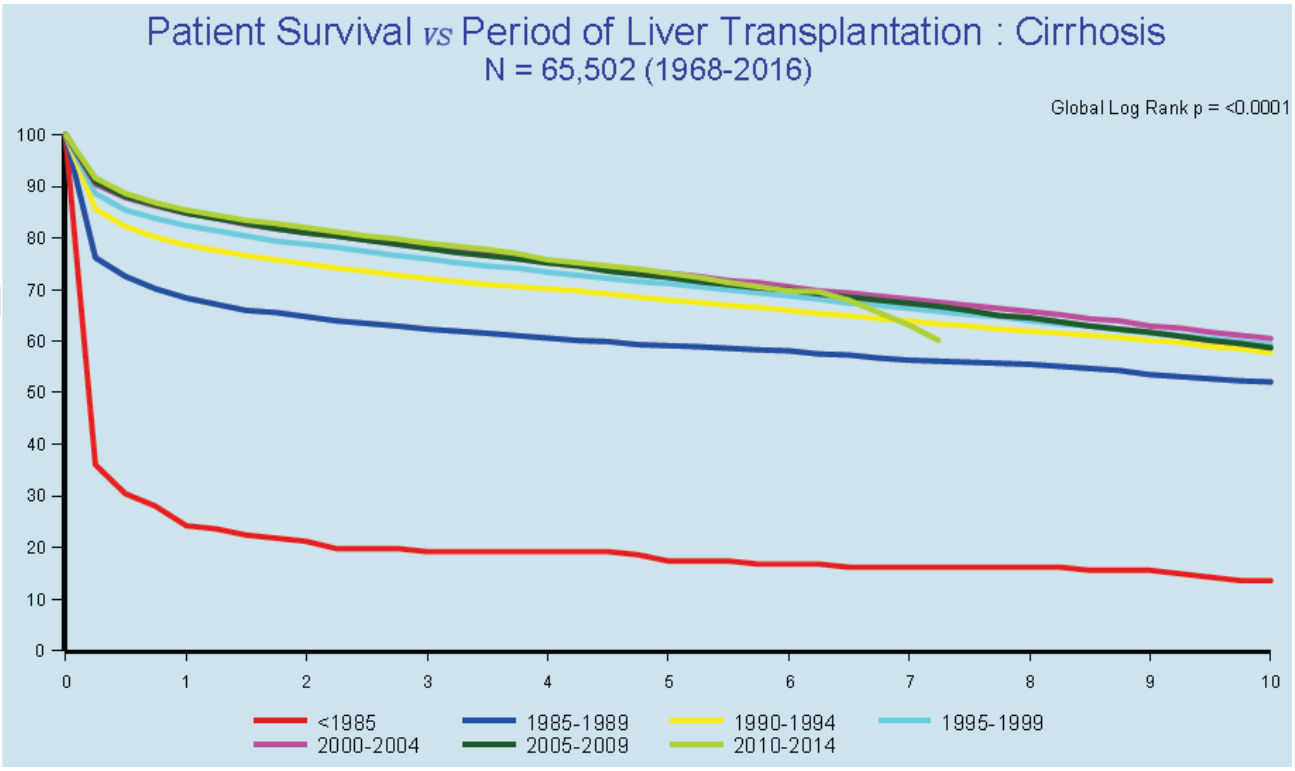


Figure 5A

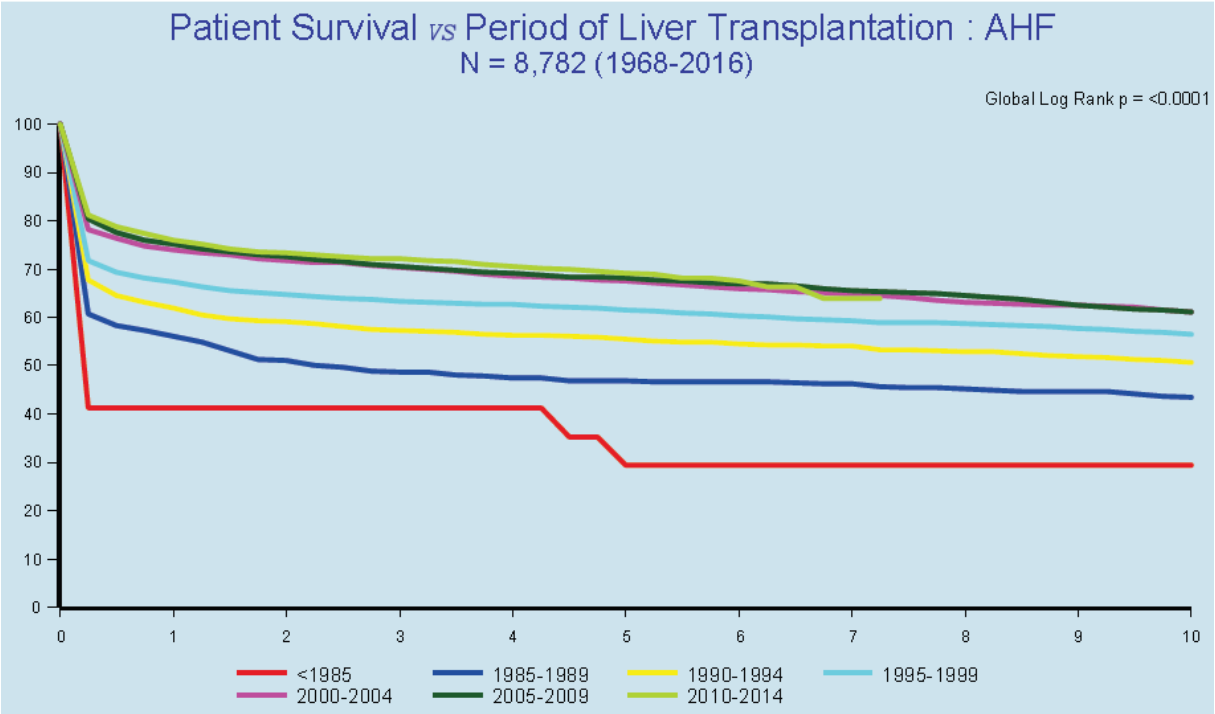


Figure 5B

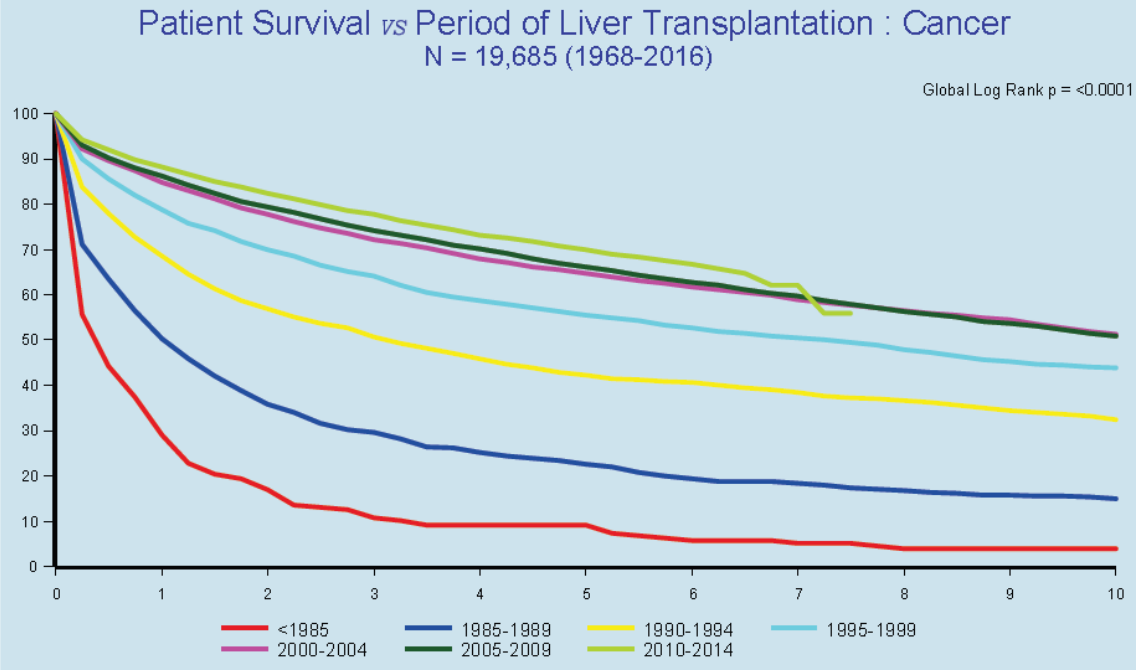
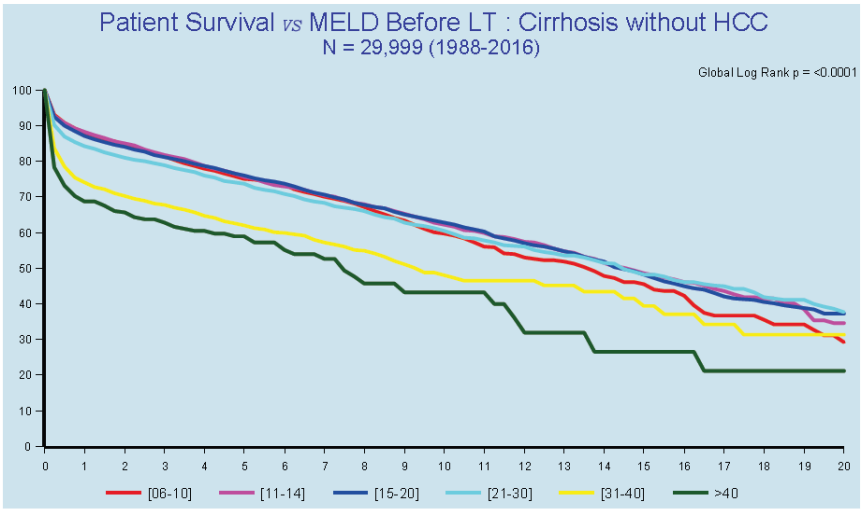


Figure 5C



Details : Log rank p

		proba
[06-10]	[11-14]	0.17
[06-10]	[15-20]	0.35
[06-10]	[21-30]	0.072
[06-10]	[31-40]	<0.0001
[06-10]	>40	<0.0001
[11-14]	[15-20]	0.58
[11-14]	[21-30]	0.0002
[11-14]	[31-40]	<0.0001
[11-14]	>40	<0.0001
[15-20]	[21-30]	0.0003
[15-20]	[31-40]	<0.0001
[15-20]	>40	<0.0001
[21-30]	[31-40]	<0.0001
[21-30]	>40	<0.0001
[31-40]	>40	0.02

Survival %

Meld_class num	1 yr	3 yrs	5 yrs	8 yrs	10 yrs	12 yrs	14 yrs	16 yrs	18 yrs	20 yrs
[06-10]	88%	81%	75%	67%	60%	53%	48%	42%	36%	29%
[11-14]	88%	82%	76%	68%	62%	57%	52%	46%	42%	35%
[15-20]	87%	81%	76%	68%	63%	57%	52%	45%	41%	37%
[21-30]	84%	79%	74%	66%	61%	56%	52%	46%	42%	38%
[31-40]	74%	68%	62%	55%	48%	46%	44%	37%	31%	31%
>40	69%	63%	59%	46%	43%	32%	27%	27%	21%	21%

Number of exposed patients

	Total	1 yr	3 yrs	5 yrs	8 yrs	10 yrs	12 yrs	14 yrs	16 yrs	18 yrs	20 yrs
[06-10]	3240	2246	1480	1076	606	374	230	120	63	29	13
[11-14]	6347	4544	3082	2159	1235	769	528	349	203	98	40
[15-20]	9856	6945	4633	3204	1661	992	687	483	290	165	64
[21-30]	7302	5042	3224	2050	981	496	325	244	164	100	38
[31-40]	2896	1807	1108	693	214	62	35	22	15	8	6
>40	358	206	121	72	24	16	7	5	5	4	1

Figure 6

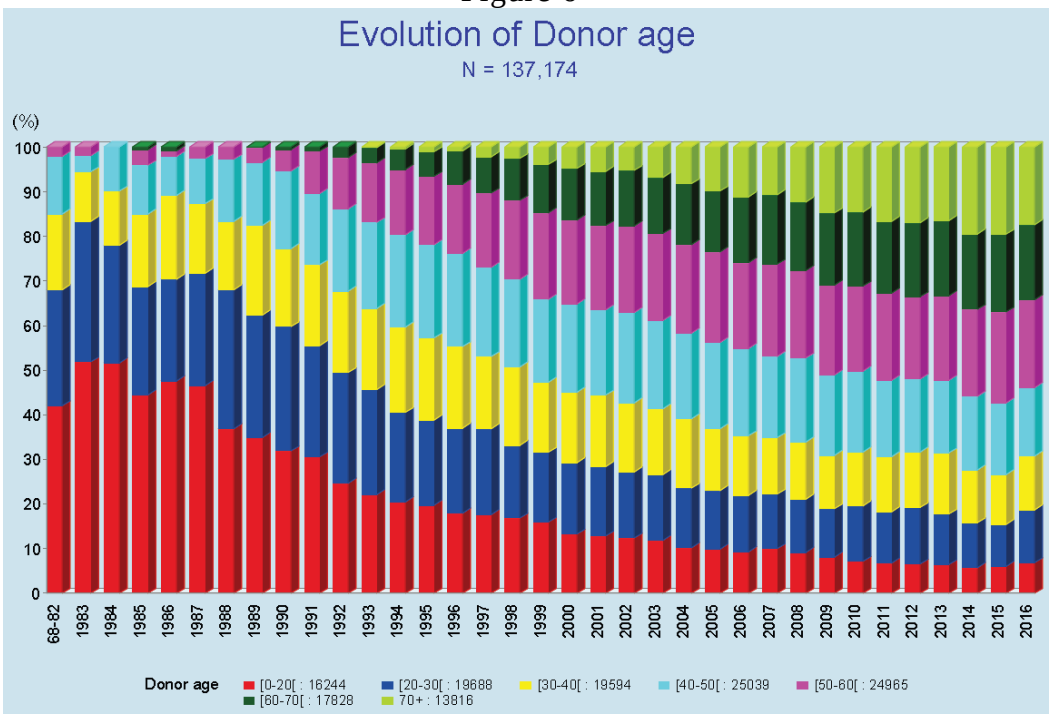
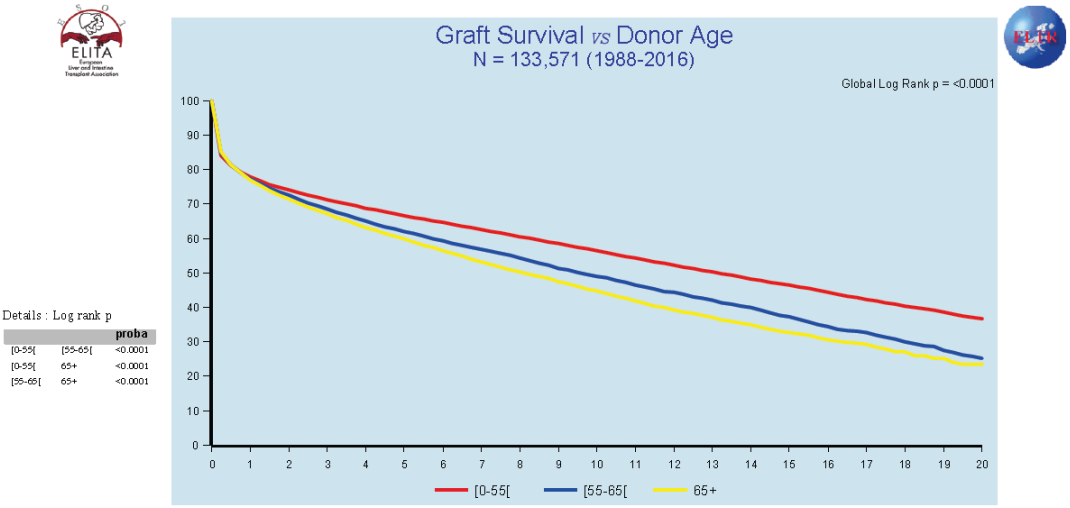


Figure 7



Survival %

3 class Donor age	1 yr	3 yrs	5 yrs	8 yrs	10 yrs	12 yrs	14 yrs	16 yrs	18 yrs	20 yrs
[0-55[	78%	71%	67%	61%	56%	52%	48%	44%	40%	37%
[55-65[	77%	68%	62%	54%	49%	44%	40%	35%	30%	25%
65+	77%	67%	60%	50%	45%	39%	35%	31%	27%	24%

Number of exposed patients

	Total	1 yr	3 yrs	5 yrs	8 yrs	10 yrs	12 yrs	14 yrs	16 yrs	18 yrs	20 yrs
[0-55[	90613	61718	47602	38474	26870	20618	15293	10929	7399	4610	2683
[55-65[	21238	14128	9969	7337	4497	3064	1956	1191	623	303	142
65+	21720	13916	8869	5765	2793	1704	932	484	222	83	24

Figure 8

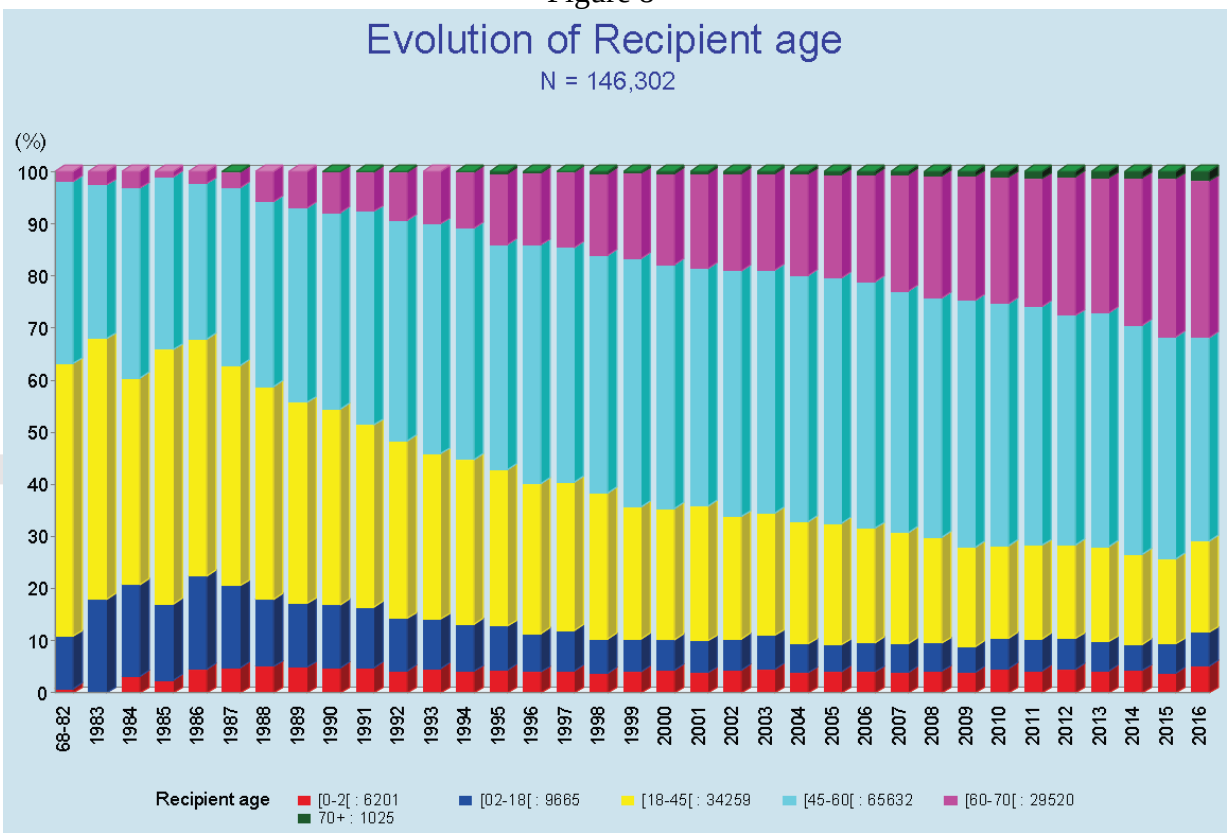
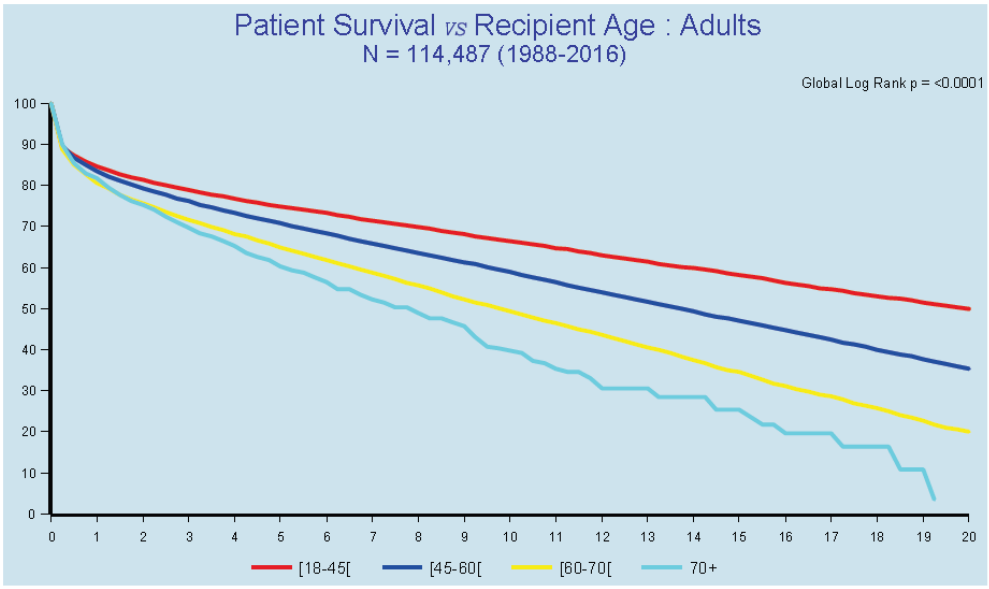


Figure 9



Details : Log rank p

		proba
[18-45[	[45-60[	<0.0001
[18-45[	[60-70[	<0.0001
[18-45[	70+	<0.0001
[45-60[	[60-70[	<0.0001
[45-60[	70+	<0.0001
[60-70[	70+	0.008

Survival %

Age of Recipient	1 yr	3 yrs	5 yrs	8 yrs	10 yrs	12 yrs	14 yrs	16 yrs	18 yrs	20 yrs
[18-45[	85%	79%	75%	70%	66%	63%	60%	56%	53%	50%
[45-60[	84%	76%	71%	64%	59%	54%	49%	45%	40%	35%
[60-70[	81%	72%	65%	56%	49%	44%	37%	31%	26%	20%
70+	82%	70%	60%	49%	40%	31%	28%	20%	16%	

Number of exposed patients

	Total	1 yr	3 yrs	5 yrs	8 yrs	10 yrs	12 yrs	14 yrs	16 yrs	18 yrs	20 yrs
[18-45[	28366	21006	16636	13820	10188	8181	6370	4910	3648	2561	1728
[45-60[	58246	42471	31927	25149	17064	12837	9258	6496	4333	2669	1549
[60-70[	26938	18351	12719	9267	5460	3758	2526	1554	867	449	219
70+	937	611	370	243	109	69	34	21	9	4	0

Figure 10

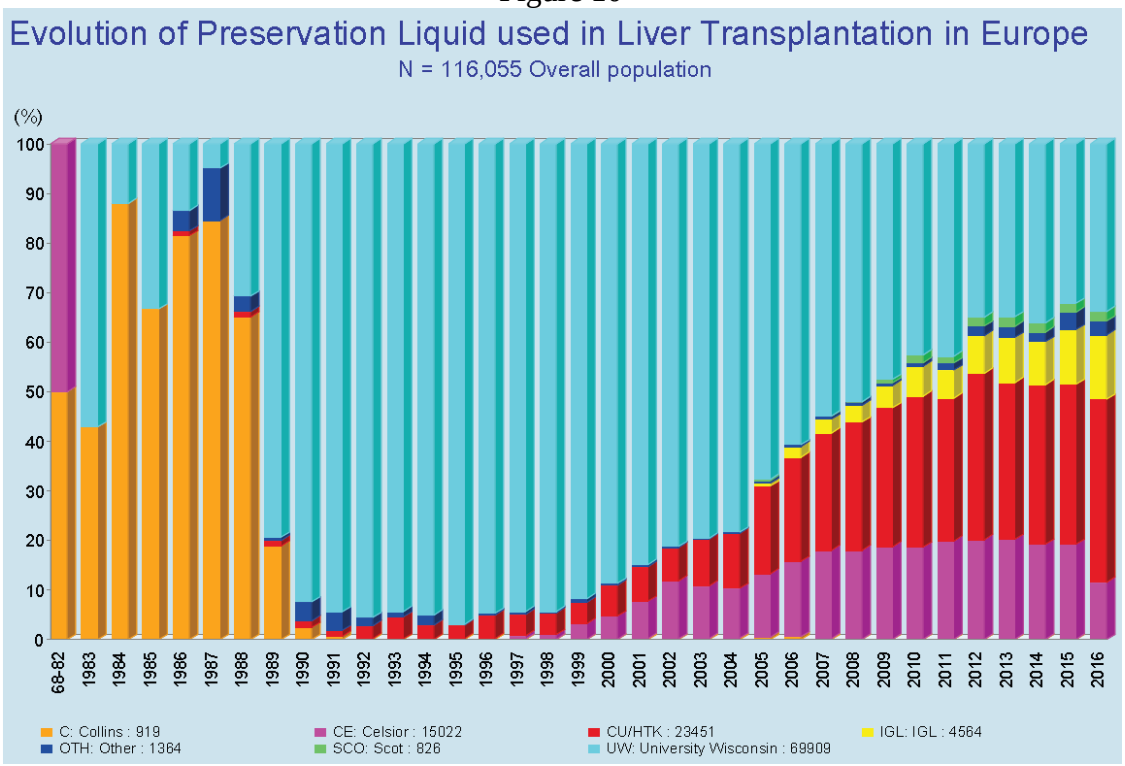
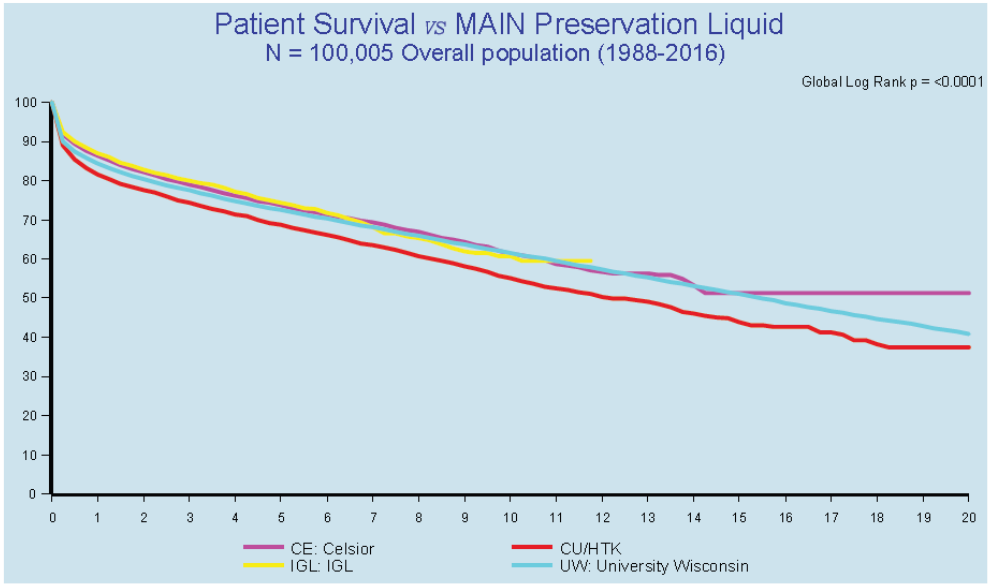


Figure 11



Details : Log rank p

		proba
UW	CU/HTK	<0.0001
UW	CE	0.0004
UW	IGL	0.014
CU/HTK	CE	<0.0001
CU/HTK	IGL	<0.0001
CE	IGL	0.85

Survival %

preserv_liq_c	1 yr	3 yrs	5 yrs	8 yrs	10 yrs	12 yrs	14 yrs	16 yrs	18 yrs	20 yrs
UW: University Wisconsin	84%	77%	72%	66%	62%	57%	53%	49%	45%	41%
CU/HTK	82%	74%	69%	61%	55%	50%	46%	43%	38%	37%
CE: Celsior	86%	79%	74%	67%	61%	57%	53%	51%	51%	51%
IGL: IGL	87%	80%	74%	65%	61%					

Number of exposed patients

	Total	1 yr	3 yrs	5 yrs	8 yrs	10 yrs	12 yrs	14 yrs	16 yrs	18 yrs	20 yrs
UW: University Wisconsin	61288	46592	37560	30864	21906	16781	12273	8669	5775	3493	1878
CU/HTK	21027	12826	7287	4613	1897	912	425	223	108	42	31
CE: Celsior	13544	9339	5797	3718	1548	703	275	85	4	3	1
IGL: IGL	4146	2722	1587	853	261	63	0	0	0	0	0

Figure 12

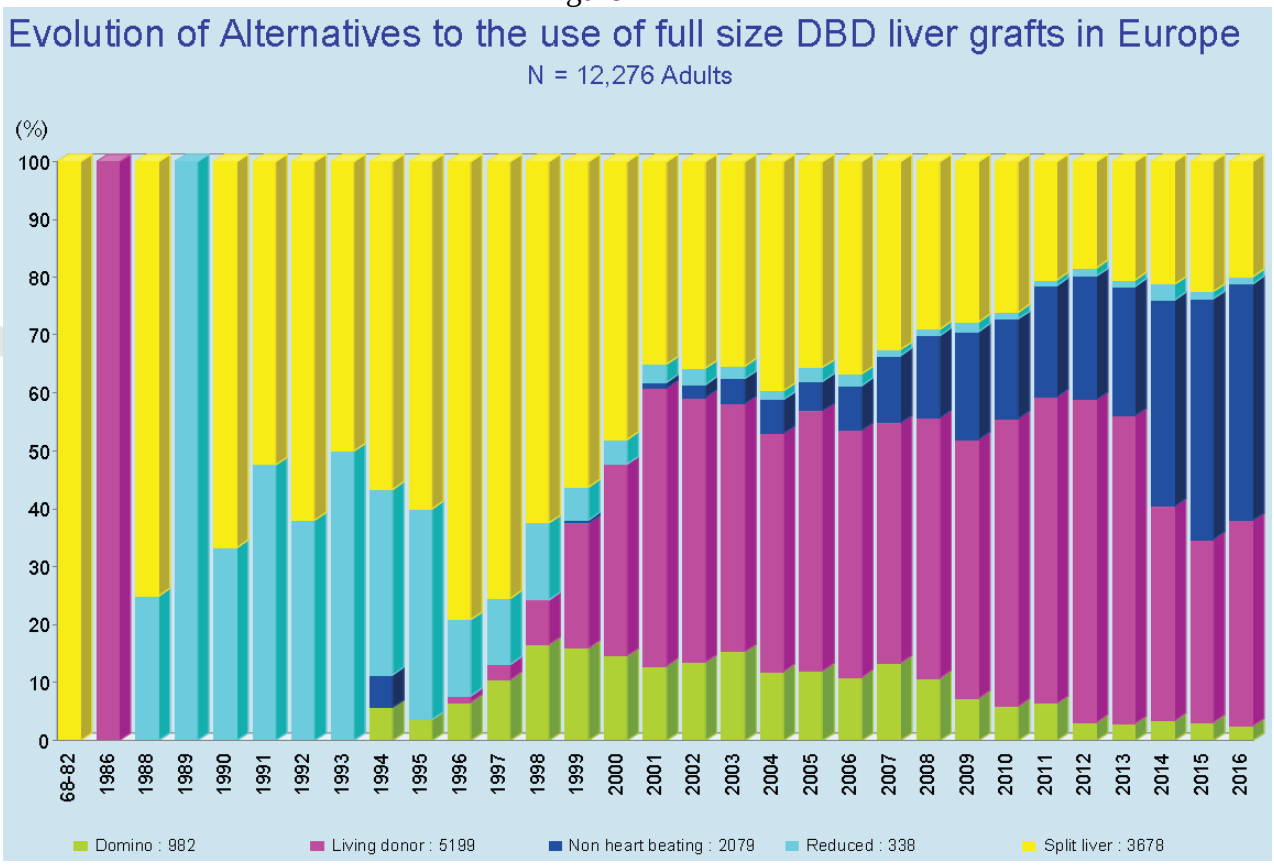
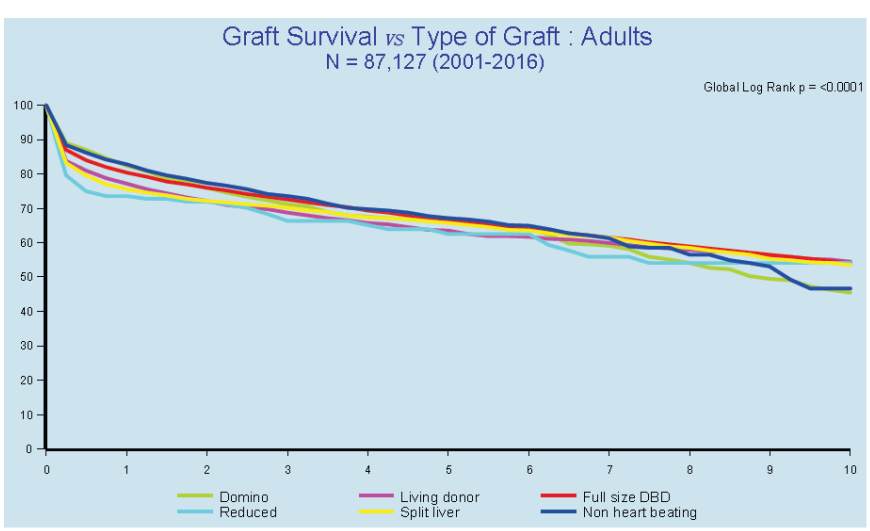


Figure 13A



Details : Log rank p

		proba
Dom.	Liv.	0.31
Dom.	FS DBD	0.006
Dom.	Red.	0.99
Dom.	Spl.	0.19
Dom.	NHB	0.29
Liv.	FS DBD	0.0002
Liv.	Red.	0.51
Liv.	Spl.	0.77
Liv.	NHB	0.004
FS DBD	Red.	0.22
FS DBD	Spl.	0.017
FS DBD	NHB	0.41
Red.	Spl.	0.59
Red.	NHB	0.18
Spl.	NHB	0.013

Survival %

Type_of_liver_graft	1 yr	2 yrs	3 yrs	4 yrs	5 yrs	6 yrs	7 yrs	8 yrs	9 yrs	10 yrs
Domino	82%	76%	71%	67%	66%	64%	59%	54%	49%	45%
Living donor	77%	72%	69%	66%	63%	62%	60%	58%	56%	54%
Full size DBD	80%	76%	72%	69%	67%	64%	61%	59%	56%	54%
Reduced	74%	72%	66%	65%	63%	63%	56%	54%	54%	54%
Split liver	75%	72%	70%	67%	66%	63%	61%	58%	55%	53%
Non heart beating	83%	77%	74%	70%	67%	65%	61%	57%	53%	47%

Number of exposed patients

	Total	1 yr	2 yrs	3 yrs	4 yrs	5 yrs	6 yrs	7 yrs	8 yrs	9 yrs	10 yrs
Domino	810	586	500	431	367	332	277	218	158	120	92
Living donor	4894	2450	1681	1325	1088	866	719	559	446	351	282
Full size DBD	76415	51605	42566	35463	30034	25490	21379	17596	14170	11141	8706
Reduced	171	99	82	66	56	44	39	31	28	24	19
Split liver	2878	1792	1521	1282	1089	960	813	656	502	378	279
Non heart beating	1959	1188	822	617	457	328	235	159	80	45	21

Figure 13B

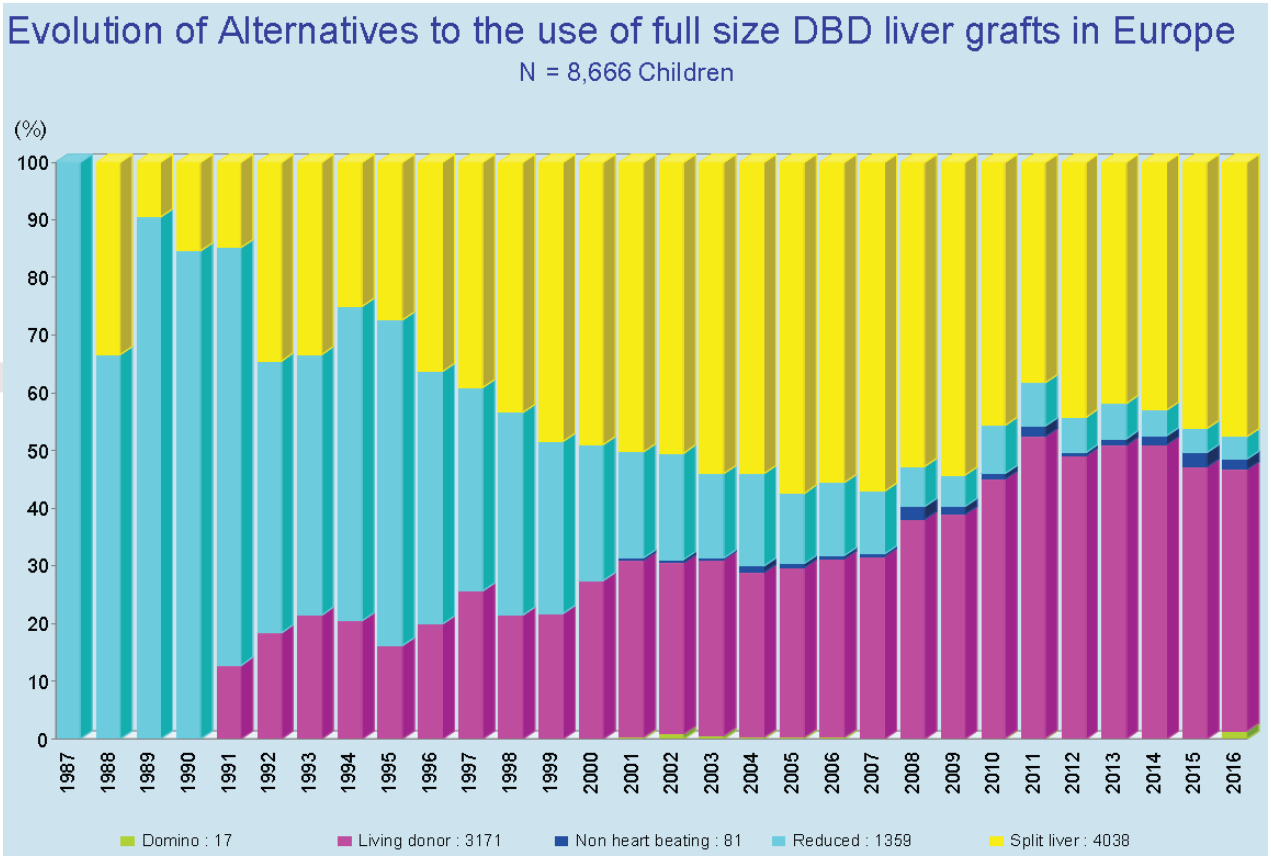
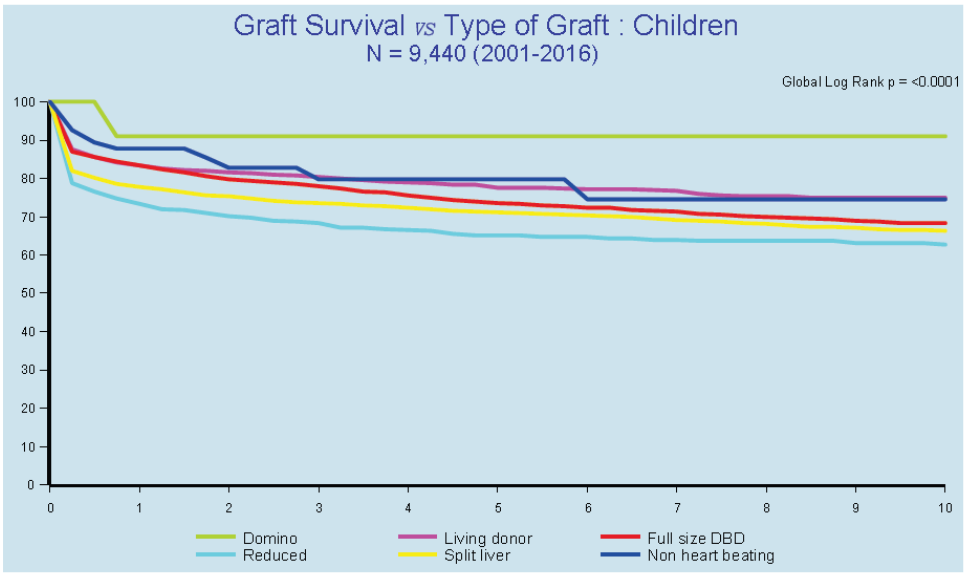


Figure 14A



Details : Log rank p

		proba
Dom.	Liv.	0.25
Dom.	FS DBD	0.2
Dom.	Red.	0.069
Dom.	Spl.	0.11
Dom.	NHB	0.43
Liv.	FS DBD	0.002
Liv.	Red.	<0.0001
Liv.	Spl.	<0.0001
Liv.	NHB	0.66
FS DBD	Red.	0.0002
FS DBD	Spl.	0.001
FS DBD	NHB	0.33
Red.	Spl.	0.044
Red.	NHB	0.023
Spl.	NHB	0.096

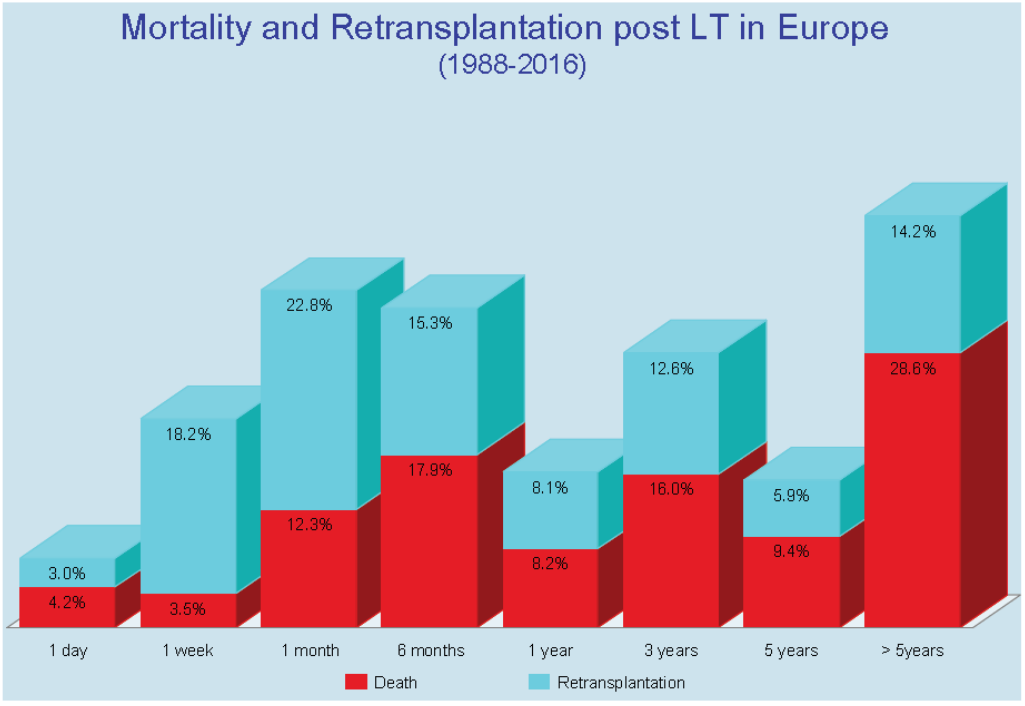
Survival %

Type_of_liver_graft	1 yr	2 yrs	3 yrs	4 yrs	5 yrs	6 yrs	7 yrs	8 yrs	9 yrs	10 yrs
Domino	91%	91%	91%	91%	91%	91%	91%	91%	91%	91%
Living donor	83%	82%	80%	79%	78%	77%	77%	75%	75%	75%
Full size DBD	83%	80%	78%	75%	74%	72%	71%	70%	69%	68%
Reduced	73%	70%	68%	66%	65%	65%	64%	64%	63%	63%
Split liver	78%	75%	74%	72%	71%	70%	69%	68%	67%	66%
Non heart beating	88%	83%	80%	80%	80%	75%	75%	75%	75%	75%

Number of exposed patients

	Total	1 yr	2 yrs	3 yrs	4 yrs	5 yrs	6 yrs	7 yrs	8 yrs	9 yrs	10 yrs
Domino	17	9	3	3	3	3	2	2	2	1	1
Living donor	2710	1518	1178	942	783	640	527	438	311	240	185
Full size DBD	2808	1936	1591	1332	1125	966	836	702	570	468	375
Reduced	594	391	348	309	272	239	206	186	166	139	115
Split liver	3241	2100	1759	1484	1277	1101	954	797	625	469	367
Non heart beating	70	45	31	26	20	19	14	11	7	5	4

Figure 14B



Cumulative proportions	1 day	1 week	1 month	6 months	1 year	3 years	5 years	>5 years
Death	4%	8%	20%	38%	46%	62%	71%	100%
Retransplantation	3%	21%	44%	59%	67%	80%	86%	100%

Figure 15

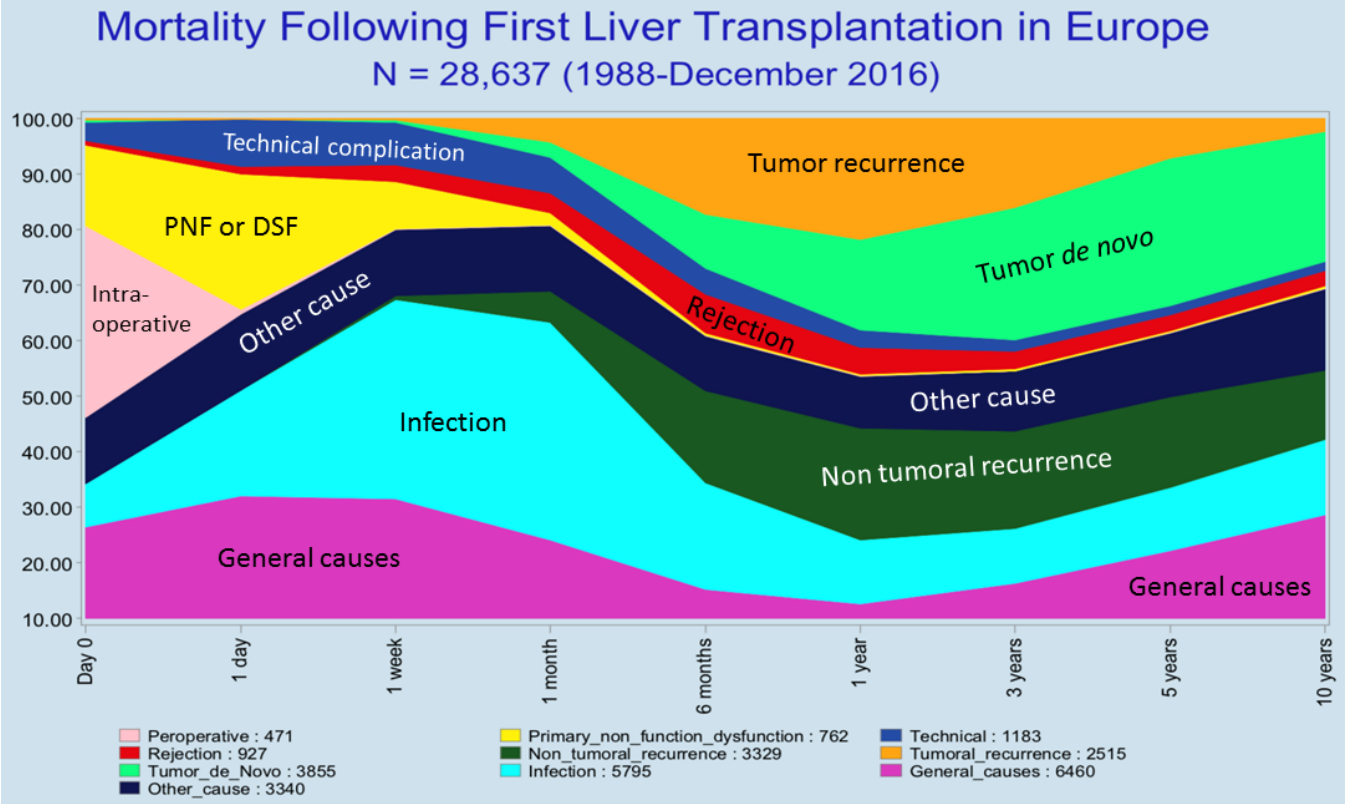
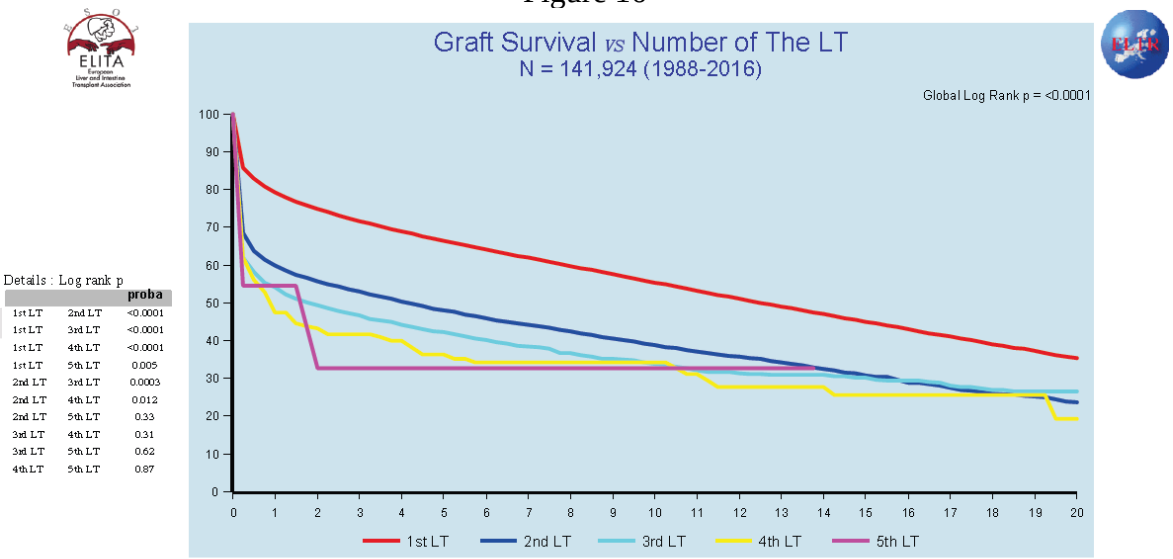


Figure 16



Details : Log rank p

		proba
1st LT	2nd LT	<0.0001
1st LT	3rd LT	<0.0001
1st LT	4th LT	<0.0001
1st LT	5th LT	0.005
2nd LT	3rd LT	0.0003
2nd LT	4th LT	0.012
2nd LT	5th LT	0.33
3rd LT	4th LT	0.31
3rd LT	5th LT	0.62
4th LT	5th LT	0.87

Survival %

Rang Th	1 yr	3 yrs	5 yrs	8 yrs	10 yrs	12 yrs	14 yrs	16 yrs	18 yrs	20 yrs
1st LT	79%	72%	66%	60%	55%	51%	47%	43%	39%	35%
2nd LT	60%	53%	48%	42%	39%	36%	33%	29%	26%	24%
3rd LT	54%	47%	42%	37%	34%	31%	31%	29%	27%	27%
4th LT	47%	42%	36%	34%	34%	28%	28%	26%	26%	19%
5th LT	55%	33%	33%	33%	33%	33%				

Number of exposed patients

	Total	1 yr	3 yrs	5 yrs	8 yrs	10 yrs	12 yrs	14 yrs	16 yrs	18 yrs	20 yrs
1st LT	128056	87625	64997	50956	34364	25974	19044	13594	9281	5944	3611
2nd LT	12241	6495	4749	3653	2437	1809	1304	923	618	407	265
3rd LT	1447	696	505	391	276	218	175	131	100	65	39
4th LT	169	71	50	36	27	24	16	13	6	5	3
5th LT	11	5	2	1	1	1	1	0	0	0	0

Figure 17

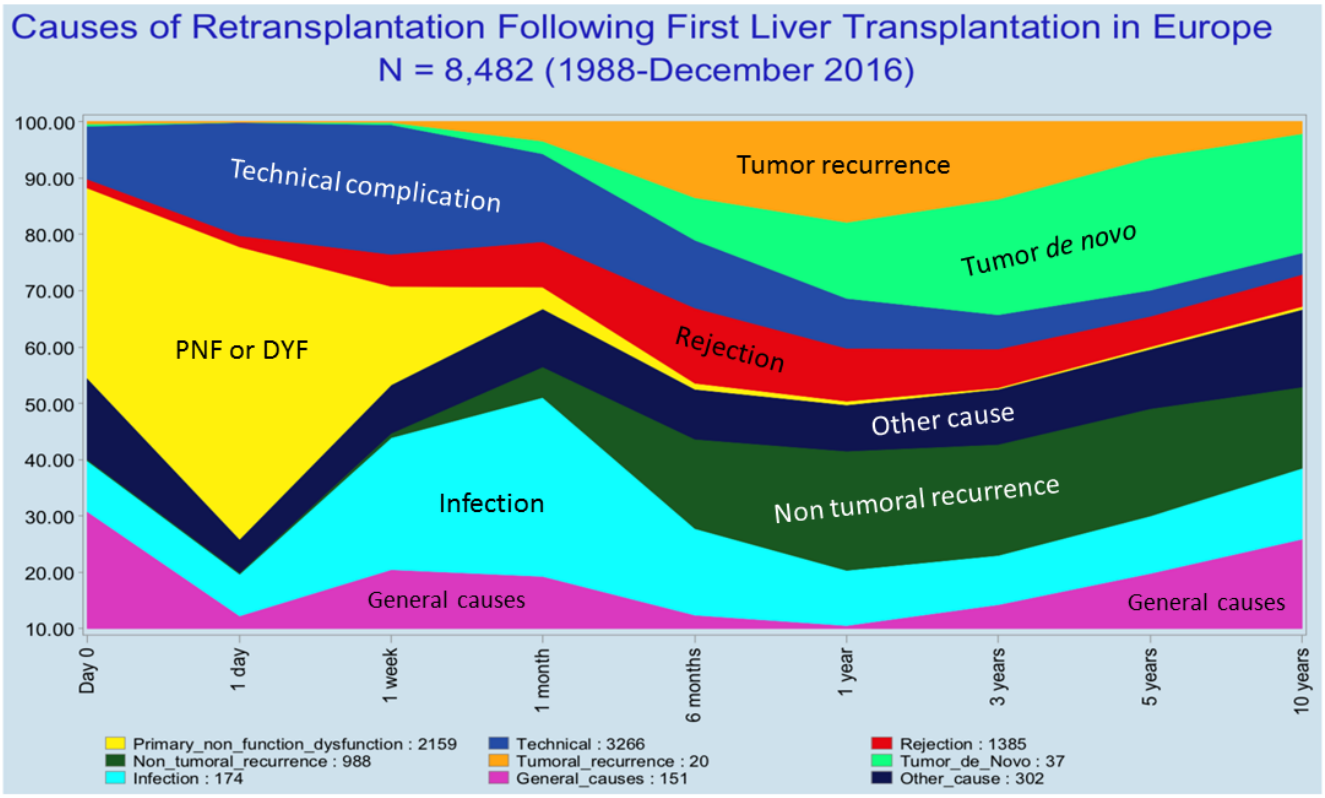
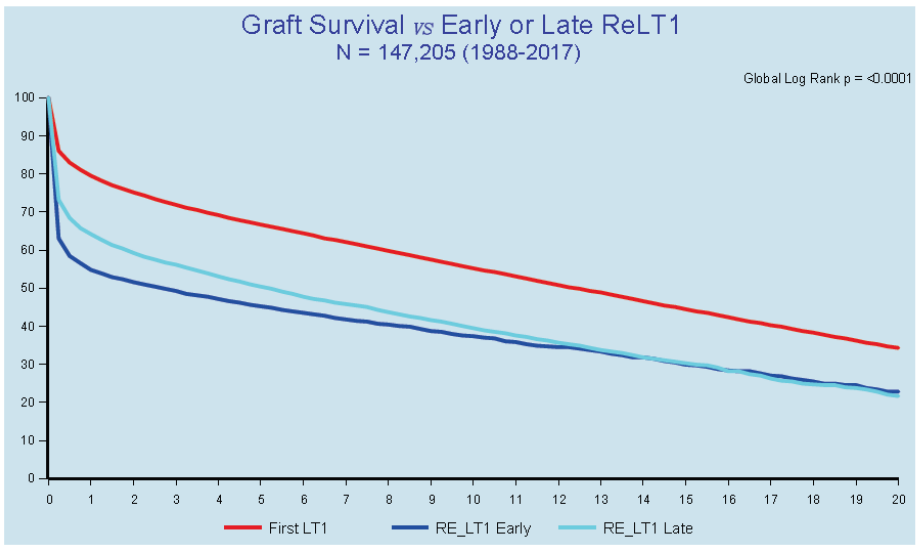


Figure 18



Details : Log rank p

		proba
First LT	RE_LT1	<0.0001
First LT	RE_LT1	<0.0001
RE_LT1	RE_LT1	<0.0001

Survival %

Rang_TH	1 yr	3 yrs	5 yrs	8 yrs	10 yrs	12 yrs	14 yrs	16 yrs	18 yrs	20 yrs
First LT1	79%	72%	67%	60%	55%	51%	47%	42%	38%	34%
RE_LT1 Early	55%	49%	45%	40%	37%	34%	32%	28%	25%	23%
RE_LT1 Late	64%	56%	50%	44%	39%	36%	32%	28%	25%	22%

Number of exposed patients

	Total	1 yr	3 yrs	5 yrs	8 yrs	10 yrs	12 yrs	14 yrs	16 yrs	18 yrs	20 yrs
First LT1	134598	91280	67979	53467	36507	27557	20414	14645	10107	6596	4039
RE_LT1 Early	5579	2670	1998	1549	1044	779	563	410	285	187	131
RE_LT1 Late	7028	3928	2878	2199	1461	1083	778	539	355	239	149

Figure 19

	From 1988 to 2016										Last 15 years									
Indication of LT	**N patients**	**% of the disease**	**% of the Total**	**Survival rate**	**N**	**1 year**	**5 years**	**10 years**	**15 years**	**20 years**	**N patients**	**% of the disease**	**% of the Total**	**Survival rate**	**N**	**1 year**	**5 years**	**10 years**	**15 years**
Acute hepatic failure	**9485**		**7%**	**Graft**	**9268**	**66%**	**58%**	**52%**	**45%**	**37%**	**6240**		**7%**	**Graft**	**6080**	**70%**	**62%**	**55%**	**46%**
				Patient	**9247**	**72%**	**65%**	**59%**	**54%**	**46%**				**Patient**	**6071**	**76%**	**69%**	**62%**	**55%**
Fulminant or Subfulminant hepatitis	**7485**		**6%**	**Graft**	**7291**	**66%**	**59%**	**53%**	**46%**	**38%**	**4606**		**5%**	**Graft**	**4466**	**71%**	**64%**	**57%**	**50%**
				Patient	**7272**	**72%**	**66%**	**60%**	**54%**	**47%**				**Patient**	**4458**	**76%**	**70%**	**64%**	**57%**
Virus A	163	2%	0.1%	Graft	160	61%	57%	52%	43%	32%	111	2%	0.1%	Graft	109	65%	61%	61%	
				Patient	159	63%	60%	56%	48%	43%				Patient	108	67%	62%	62%	
Virus B	917	12%	1%	Graft	909	69%	62%	57%	50%	40%	578	13%	1%	Graft	571	74%	67%	64%	52%
				Patient	905	75%	68%	63%	57%	47%				Patient	570	78%	73%	69%	61%
Virus C	127	2%	0.1%	Graft	125	65%	53%	39%	32%	25%	80	2%	0.1%	Graft	78	68%	50%	35%	
				Patient	125	72%	58%	42%	39%	27%				Patient	78	74%	54%	40%	
Virus D	14	0.2%	0.01%	Graft	14	76%	67%	46%	46%	46%	4	0.1%	0.004%	Graft	4	100%	100%	67%	67%
				Patient	14	76%	67%	56%	56%	56%				Patient	4	100%	100%	100%	100%
Other known	797	11%	1%	Graft	776	68%	61%	56%	49%	40%	565	12%	1%	Graft	547	71%	64%	57%	
				Patient	776	73%	68%	64%	55%	48%				Patient	547	76%	71%	64%	
Other unknown	3647	49%	3%	Graft	3585	65%	58%	53%	46%	39%	1966	43%	2%	Graft	1922	71%	65%	59%	50%
				Patient	3576	71%	65%	60%	55%	48%				Patient	1918	77%	71%	65%	57%
Paracetamol	743	10%	1%	Graft	671	69%	59%	50%	45%	32%	531	12%	1%	Graft	477	74%	64%	53%	43%
				Patient	668	74%	65%	58%	54%	43%				Patient	476	78%	70%	63%	59%
Other drug related: specify	715	10%	1%	Graft	692	68%	62%	49%	44%	35%	472	10%	1%	Graft	461	72%	66%	56%	56%
				Patient	691	72%	67%	56%	50%	42%				Patient	461	77%	71%	61%	61%

Toxic (non drug)	362	5%	0.3%	Graft	359	63%	58%	51%	44%	29%	299	6%	0.3%	Graft	297	63%	58%	48%	48%
				Patient	358	68%	64%	58%	51%	45%				Patient	296	68%	63%	54%	54%
Traumatic acute hepatic failure	**430**		**0.3%**	**Graft**	**430**	**48%**	**39%**	**35%**	**31%**	**31%**	**346**		**0.4%**	**Graft**	**346**	**52%**	**41%**	**36%**	
				Patient	**429**	**57%**	**48%**	**44%**	**43%**	**43%**				**Patient**	**346**	**61%**	**51%**	**44%**	
Post operative	173	40%	0.1%	Graft	173	30%	20%	17%			138	40%	0.2%	Graft	138	33%	21%	17%	
				Patient	173	45%	34%	29%	24%	24%				Patient	138	48%	38%	30%	
Post traumatic	257	60%	0.2%	Graft	257	61%	52%	48%	45%	45%	208	60%	0.2%	Graft	208	65%	55%	49%	
				Patient	256	65%	57%	54%	54%	54%				Patient	208	69%	60%	54%	
Subacute hepatic failure	**1570**		**1%**								**1288**		**1%**						
Virus A	10	1%	0.01%	Graft	10	67%	50%				8	1%	0.01%	Graft	8	71%	48%		
				Patient	10	67%	50%							Patient	8	71%	48%		
Virus B	130	8%	0.1%	Graft	127	80%	65%	54%	20%		113	9%	0.1%	Graft	111	80%	68%	63%	
				Patient	127	85%	67%	61%	49%					Patient	111	85%	72%	66%	66%
Virus C	184	12%	0.1%	Graft	184	75%	56%	32%	18%		161	13%	0.2%	Graft	161	75%	55%	33%	
				Patient	183	78%	60%	36%	28%					Patient	160	79%	58%	34%	
Virus D	6	0.4%	0.005%	Graft	6	67%	67%	67%			4	0.3%	0.004%	Graft	4	75%	75%	75%	
				Patient	6	83%	83%	56%						Patient	4	75%	75%	75%	
Other known	62	4%	0.05%	Graft	61	76%	66%	66%	66%	66%	54	4%	0.1%	Graft	53	80%	68%	68%	
				Patient	61	79%	71%	64%	64%	64%				Patient	53	84%	74%	63%	
Other unknown	278	18%	0.2%	Graft	267	77%	67%	62%	55%	45%	207	16%	0.2%	Graft	198	80%	71%	67%	58%
				Patient	267	81%	75%	71%	65%	53%				Patient	198	84%	79%	76%	64%
Paracetamol	5	0.3%	0.004%	Graft	5	67%	67%				4	0.3%	0.004%	Graft	4	100%	100%		
				Patient	5	67%	67%							Patient	4	100%	100%		
Other drug related: specify	60	4%	0.05%	Graft	56	62%	55%	49%	41%	41%	51	4%	0.1%	Graft	47	66%	57%	53%	
				Patient	56	70%	65%	56%	49%	49%				Patient	47	70%	65%	55%	

Toxic (non drug)	24	2%	0.02%	Graft	23	78%	68%	54%	27%		17	1%	0.02%	Graft	16	87%	80%	80%	
				Patient	23	78%	73%	58%	58%					Patient	16	87%	87%	87%	
Other acute hepatic failure: specify	811	52%	1%	Graft	808	65%	54%	46%	40%	29%	669	52%	1%	Graft	666	67%	53%	46%	25%
				Patient	808	72%	63%	55%	51%	45%				Patient	666	74%	62%	54%	48%
Fulminant or subfulminant or subacute hepatitis	**11625**		**9%**								**7638**		**8%**						
Viral	1551	13%	1%	Graft	1535	70%	60%	53%	45%	36%	1054	14%	1%	Graft	1046	73%	63%	57%	46%
				Patient	1529	75%	66%	58%	52%	43%				Patient	1043	78%	68%	61%	55%
Virus B	1047	9%	1%	Graft	1036	71%	62%	57%	49%	40%	691	9%	1%	Graft	682	75%	67%	64%	51%
				Patient	1032	76%	69%	63%	57%	47%				Patient	681	80%	73%	69%	61%
Drug-related	1523	13%	1%	Graft	1424	68%	60%	50%	44%	34%	1058	14%	1%	Graft	989	73%	65%	55%	50%
				Patient	1420	73%	66%	57%	52%	43%				Patient	988	77%	70%	62%	60%
Paracetamol	748	6%	1%	Graft	676	69%	59%	50%	45%	32%	535	7%	1%	Graft	481	75%	64%	53%	43%
				Patient	673	74%	65%	58%	54%	43%				Patient	480	78%	70%	63%	59%
Other drugs	775	7%	1%	Graft	748	68%	61%	49%	44%	35%	523	7%	1%	Graft	508	72%	65%	56%	56%
				Patient	747	72%	66%	56%	50%	42%				Patient	508	76%	70%	61%	61%
Toxic (non drug)	386	3%	0.3%	Graft	382	64%	59%	51%	44%	29%	316	4%	0.3%	Graft	313	64%	59%	49%	46%
				Patient	381	69%	65%	58%	51%	45%				Patient	312	69%	65%	56%	56%
Unknown or others	5595	48%	4%	Graft	5497	66%	59%	53%	47%	39%	3461	45%	4%	Graft	3386	71%	63%	57%	46%
				Patient	5488	72%	66%	61%	55%	48%				Patient	3382	77%	70%	64%	55%
Cholestatic disease	**13241**		**10%**	**Graft**	**12917**	**82%**	**73%**	**62%**	**50%**	**38%**	**8439**		**9%**	**Graft**	**8242**	**84%**	**74%**	**63%**	**52%**
				Patient	**12883**	**87%**	**79%**	**71%**	**59%**	**46%**				**Patient**	**8221**	**90%**	**81%**	**73%**	**62%**
Secondary biliary cirrhosis	976	7%	1%	Graft	955	72%	62%	54%	47%	39%	693	8%	1%	Graft	679	73%	62%	54%	49%
				Patient	955	79%	69%	62%	56%	48%				Patient	679	80%	69%	63%	58%
Primary biliary cholangitis	5865	44%	5%	Graft	5698	83%	76%	66%	54%	41%	3050	36%	3%	Graft	2971	86%	78%	68%	59%
				Patient	5688	87%	80%	71%	58%	45%				Patient	2966	90%	83%	74%	64%

Primary sclerosing cholangitis	5786	44%	5%	Graft	5682	83%	71%	58%	45%	31%	4248	50%	5%	Graft	4172	85%	73%	59%	46%
				Patient	5663	89%	80%	71%	60%	46%				Patient	4160	91%	82%	74%	60%
Other cholestatic disease: specify	614	5%	0.5%	Graft	582	80%	74%	68%	58%	50%	448	5%	0.5%	Graft	420	79%	71%	66%	62%
				Patient	577	86%	82%	78%	69%	64%				Patient	416	86%	80%	77%	71%
Congenital biliary disease	**6397**		**5%**	**Graft**	**6248**	**82%**	**77%**	**73%**	**68%**	**63%**	**4274**		**5%**	**Graft**	**4180**	**85%**	**81%**	**77%**	**68%**
				Patient	**6234**	**88%**	**85%**	**83%**	**80%**	**76%**				**Patient**	**4174**	**91%**	**88%**	**87%**	**85%**
Caroli disease	258	4%	0.2%	Graft	257	81%	74%	66%	57%	52%	207	5%	0.2%	Graft	206	82%	74%	62%	
				Patient	257	89%	84%	80%	70%	66%				Patient	206	90%	86%	78%	78%
Extrahepatic biliary atresia	5232	82%	4%	Graft	5107	82%	77%	74%	70%	64%	3403	80%	4%	Graft	3326	86%	82%	78%	74%
				Patient	5095	89%	85%	83%	81%	78%				Patient	3322	92%	89%	88%	86%
Congenital biliary fibrosis	194	3%	0.2%	Graft	192	80%	77%	67%	63%	61%	138	3%	0.2%	Graft	136	83%	78%	66%	66%
				Patient	192	88%	85%	75%	71%	69%				Patient	136	90%	88%	75%	75%
Choledocal cyst	41	1%	0.03%	Graft	41	87%	80%	54%	36%		21	0.5%	0.02%	Graft	21	79%	63%	42%	
				Patient	41	87%	87%	76%	76%					Patient	21	79%	79%	59%	
Alagille syndrome	338	5%	0.3%	Graft	335	82%	77%	74%	69%	69%	261	6%	0.3%	Graft	258	85%	81%	79%	75%
				Patient	335	88%	84%	80%	77%	72%				Patient	258	90%	87%	85%	80%
Other congenital biliary disease: specify	334	5%	0.3%	Graft	316	83%	75%	68%	54%	44%	244	6%	0.3%	Graft	233	83%	75%	70%	21%
				Patient	314	88%	81%	78%	68%	62%				Patient	231	89%	83%	82%	75%
Cirrhosis	**64166**		**50%**	**Graft**	**63140**	**80%**	**67%**	**55%**	**43%**	**32%**	**45566**		**50%**	**Graft**	**44806**	**82%**	**68%**	**55%**	**42%**
				Patient	**63062**	**84%**	**71%**	**59%**	**47%**	**36%**				**Patient**	**44758**	**85%**	**72%**	**59%**	**46%**
Alcoholic cirrhosis	24380	38%	19%	Graft	24030	82%	70%	55%	41%	29%	18135	40%	20%	Graft	17849	83%	71%	55%	40%
				Patient	24005	85%	74%	58%	43%	31%				Patient	17830	86%	75%	59%	43%
Autoimmune Cirrhosis	2929	5%	2%	Graft	2850	81%	71%	60%	48%	38%	2027	4%	2%	Graft	1978	83%	74%	63%	45%
				Patient	2843	86%	77%	68%	57%	48%				Patient	1974	88%	80%	72%	57%
Virus B related cirrhosis	5822	9%	5%	Graft	5746	80%	70%	64%	56%	48%	3826	8%	4%	Graft	3774	82%	72%	66%	57%

				Patient	5739	84%	74%	68%	61%	52%				Patient	3770	86%	76%	70%	62%
Virus C related cirrhosis	15187	24%	12%	Graft	15062	77%	60%	47%	37%	26%	10495	23%	12%	Graft	10396	78%	59%	46%	36%
				Patient	15051	80%	64%	52%	41%	30%				Patient	10387	81%	64%	51%	40%
Virus BD related cirrhosis	1939	3%	2%	Graft	1899	89%	84%	79%	74%	67%	1431	3%	2%	Graft	1403	89%	84%	79%	75%
				Patient	1895	92%	88%	84%	81%	73%				Patient	1401	93%	89%	83%	78%
Virus BC related cirrhosis	829	1%	1%	Graft	819	78%	64%	54%	42%	31%	559	1%	1%	Graft	552	80%	66%	54%	34%
				Patient	818	82%	70%	60%	47%	33%				Patient	551	83%	71%	60%	39%
Virus BCD related cirrhosis	174	0.3%	0.1%	Graft	170	88%	78%	62%	47%	47%	134	0.3%	0.1%	Graft	130	88%	78%	67%	
				Patient	170	90%	80%	67%	45%	45%				Patient	130	89%	81%	69%	
Virus related cirrhosis-Other viruses: specify	1994	3%	2%	Graft	1780	83%	64%	49%	35%	24%	1353	3%	1%	Graft	1208	86%	66%	52%	39%
				Patient	1766	85%	68%	54%	40%	27%				Patient	1203	89%	71%	57%	44%
Combined virus C and alcoholic cirrhosis	1996	3%	2%	Graft	1980	82%	65%	50%	36%	24%	1531	3%	2%	Graft	1515	83%	66%	51%	38%
				Patient	1980	85%	69%	55%	41%	27%				Patient	1516	86%	70%	56%	44%
Combined virus B and alcoholic cirrhosis	489	1%	0.4%	Graft	485	87%	74%	61%	53%	53%	382	1%	0.4%	Graft	379	88%	77%	68%	
				Patient	484	90%	78%	64%	55%	55%				Patient	379	91%	80%	70%	
Post hepatitic cirrhosis-Drug related	77	0.1%	0.1%	Graft	77	78%	63%	46%	33%		44	0.1%	0.05%	Graft	44	84%	65%		
				Patient	77	79%	67%	52%	34%					Patient	44	84%	70%	34%	
Other cirrhosis: specify	2732	4%	2%	Graft	2728	77%	64%	55%	47%	38%	1841	4%	2%	Graft	1837	78%	66%	55%	45%
				Patient	2727	81%	69%	59%	51%	42%				Patient	1836	83%	71%	59%	48%
Cryptogenic (unknown) cirrhosis	5618	9%	4%	Graft	5514	78%	67%	56%	46%	34%	3808	8%	4%	Graft	3741	80%	69%	57%	45%
				Patient	5507	81%	72%	61%	50%	37%				Patient	3737	83%	73%	61%	47%
Primary liver tumors	**21135**		**17%**	**Graft**	**20976**	**81%**	**60%**	**47%**	**36%**	**28%**	**17329**		**19%**	**Graft**	**17206**	**83%**	**64%**	**49%**	**37%**
				Patient	**20971**	**84%**	**64%**	**50%**	**39%**	**31%**				**Patient**	**17202**	**87%**	**67%**	**53%**	**40%**
Hepatocellular carcinoma and cirrhosis	18349	87%	14%	Graft	18225	82%	62%	48%	36%	28%	15617	90%	17%	Graft	15510	84%	65%	49%	38%
				Patient	18220	86%	66%	51%	39%	31%				Patient	15506	87%	68%	53%	40%

Hepatocellular carcinoma and non cirrhotic liver	734	3%	1%	Graft	726	72%	49%	34%	24%	18%	425	2%	0.5%	Graft	423	81%	61%	44%	
				Patient	726	77%	52%	37%	27%	20%				Patient	423	87%	66%	48%	24%
Hepatocellular carcinoma - Fibrolamellar	51	0.2%	0.04%	Graft	51	76%	38%	33%	27%	27%	26	0.2%	0.03%	Graft	26	85%	45%		
				Patient	51	80%	41%	36%	36%	36%				Patient	26	88%	47%		
Biliary tract carcinoma (Klatskin)	395	2%	0.3%	Graft	394	65%	34%	26%	16%	13%	245	1%	0.3%	Graft	244	67%	35%	25%	
				Patient	394	72%	41%	35%	24%	21%				Patient	244	76%	47%	41%	
Hepatic cholangiocellular carcinoma	530	3%	0.4%	Graft	526	66%	32%	23%	16%	14%	306	2%	0.3%	Graft	306	73%	40%	31%	17%
				Patient	526	69%	33%	25%	19%	15%				Patient	306	77%	42%	32%	22%
Hepatoblastoma	377	2%	0.3%	Graft	372	83%	75%	71%	70%	61%	330	2%	0.4%	Graft	325	84%	77%	73%	73%
				Patient	372	87%	80%	77%	75%	66%				Patient	325	88%	83%	79%	79%
Epithelioid hemangioendothelioma	216	1%	0.2%	Graft	213	85%	72%	67%	61%	58%	161	1%	0.2%	Graft	158	85%	73%	65%	60%
				Patient	213	90%	77%	71%	67%	60%				Patient	158	91%	79%	71%	65%
Angiosarcoma	17	0.1%	0.01%	Graft	17	35%					3	0.02%	0.003%	Graft	3	67%			
				Patient	17	38%								Patient	3	67%			
Other liver malignancies: specify	466	2%	0.4%	Graft	452	70%	46%	40%	33%	28%	216	1%	0.2%	Graft	211	82%	62%	57%	
				Patient	452	73%	49%	44%	36%	31%				Patient	211	85%	65%	62%	
Secondary liver tumors	**639**		**0.5%**	**Graft**	**636**	**75%**	**48%**	**32%**	**24%**	**19%**	**395**		**0.4%**	**Graft**	**393**	**79%**	**57%**	**44%**	**33%**
				Patient	**636**	**80%**	**52%**	**34%**	**26%**	**21%**				**Patient**	**393**	**85%**	**61%**	**46%**	**36%**
Carcinoid	341	53%	0.3%	Graft	339	78%	52%	34%	24%	19%	185	47%	0.2%	Graft	183	83%	64%	51%	38%
				Patient	339	82%	55%	36%	27%	22%				Patient	183	87%	67%	54%	41%
Other neuroendocrine	188	29%	0.1%	Graft	188	74%	51%	40%	34%		140	35%	0.2%	Graft	140	76%	56%	44%	36%
				Patient	188	80%	56%	43%	35%					Patient	140	83%	61%	45%	37%
Colorectal	73	11%	0.1%	Graft	72	73%	24%	3%			53	13%	0.1%	Graft	53	81%	24%		
				Patient	72	80%	26%	3%						Patient	53	85%	29%		
GI non colorectal	18	3%	0.01%	Graft	18	60%	35%	20%	10%		8	2%	0.01%	Graft	8	45%	23%	23%	23%

				Patient	18	60%	35%	20%	10%					Patient	8	45%	23%	23%	23%
Non gastrointestinal	19	3%	0.01%	Graft	19	61%	41%	20%			9	2%	0.01%	Graft	9	76%	57%		
				Patient	19	72%	50%	27%						Patient	9	100%	80%		
Metabolic disease	**7414**		**6%**	**Graft**	**7188**	**82%**	**73%**	**64%**	**55%**	**48%**	**5336**		**6%**	**Graft**	**5166**	**83%**	**74%**	**63%**	**52%**
				Patient	**7163**	**87%**	**79%**	**71%**	**63%**	**56%**				**Patient**	**5147**	**88%**	**80%**	**71%**	**60%**
Wilson disease	1241	17%	1%	Graft	1200	83%	78%	71%	64%	56%	904	17%	1%	Graft	879	85%	79%	72%	65%
				Patient	1191	89%	86%	81%	76%	69%				Patient	875	92%	87%	82%	77%
Hemochromatosis	622	8%	0.5%	Graft	610	74%	63%	48%	36%	28%	399	7%	0.4%	Graft	390	77%	65%	47%	40%
				Patient	609	77%	66%	51%	38%	29%				Patient	389	80%	69%	50%	41%
Alpha-1 - Antitrypsin deficiency	717	10%	1%	Graft	678	83%	75%	66%	58%	44%	478	9%	1%	Graft	457	84%	76%	68%	54%
				Patient	678	87%	81%	72%	65%	56%				Patient	457	88%	81%	73%	61%
Glycogen storage disease	145	2%	0.1%	Graft	142	87%	84%	77%	68%	68%	118	2%	0.1%	Graft	115	88%	83%	69%	
				Patient	142	94%	92%	86%	76%	76%				Patient	115	95%	92%	81%	
Homozygous Hypercholesterolemia	36	0.5%	0.03%	Graft	36	86%	81%	65%	65%	65%	29	1%	0.03%	Graft	29	85%	80%		
				Patient	36	86%	81%	81%	81%	81%				Patient	29	85%	80%		
Tyrosinemia	122	2%	0.1%	Graft	119	85%	75%	73%	71%	65%	65	1%	0.1%	Graft	62	87%	84%	84%	
				Patient	118	91%	86%	84%	84%	84%				Patient	62	90%	87%	87%	
Familial amyloidotic polyneuropathy	1261	17%	1%	Graft	1241	82%	73%	62%	50%	38%	866	16%	1%	Graft	847	83%	73%	62%	50%
				Patient	1231	88%	79%	68%	56%	46%				Patient	837	90%	81%	69%	
Primary hyperoxaluria	332	4%	0.3%	Graft	326	79%	72%	62%	53%	50%	264	5%	0.3%	Graft	258	78%	73%	61%	33%
				Patient	326	84%	77%	68%	58%	58%				Patient	258	84%	79%	67%	25%
Protoporphyria	19	0.3%	0.01%	Graft	19	77%	77%	70%	61%	51%	8	0.1%	0.01%	Graft	8	69%	69%		
				Patient	19	77%	77%	70%	61%	51%				Patient	8	69%	69%		
Other porphyria	17	0.2%	0.01%	Graft	17	81%	65%	65%			13	0.2%	0.01%	Graft	13	83%	83%		
				Patient	17	87%	65%	65%						Patient	13	91%	82%		
Non alcoholic steatohepatitis (NASH)	749	10%	1%	Graft	706	83%	72%	51%			748	14%	1%	Graft	705	83%	72%	52%	

				Patient	705	86%	75%	54%						Patient	704	86%	75%	55%	
Crigler-Najjar	93	1%	0.1%	Graft	88	86%	74%	72%	72%	72%	65	1%	0.1%	Graft	60	84%	70%	66%	
				Patient	88	94%	89%	89%	89%	89%				Patient	60	95%	91%	91%	
Cystic fibrosis	277	4%	0.2%	Graft	272	83%	68%	63%	57%	46%	233	4%	0.3%	Graft	228	86%	73%	68%	
				Patient	271	85%	74%	64%	57%	45%				Patient	227	88%	76%	70%	
Byler disease	251	3%	0.2%	Graft	250	85%	81%	78%	71%	71%	137	3%	0.2%	Graft	136	88%	82%	74%	59%
				Patient	250	94%	92%	89%	85%	85%				Patient	136	94%	92%	90%	79%
Other metabolic disease	1532	21%	1%	Graft	1484	81%	71%	63%	55%	49%	1009	19%	1%	Graft	979	83%	72%	63%	54%
				Patient	1482	86%	77%	71%	63%	57%				Patient	977	88%	79%	72%	65%
Budd Chiari	**1069**		**1%**	**Graft**	**1052**	**73%**	**65%**	**57%**	**49%**	**39%**	**715**		**1%**	**Graft**	**704**	**77%**	**67%**	**58%**	**49%**
				Patient	**1051**	**79%**	**72%**	**65%**	**57%**	**49%**				**Patient**	**704**	**82%**	**74%**	**65%**	**57%**
													0%						
Benign liver tumors or Polycystic disease	**1824**		**1%**	**Graft**	**1804**	**85%**	**80%**	**70%**	**60%**	**52%**	**1516**		**2%**	**Graft**	**1499**	**87%**	**81%**	**71%**	**60%**
				Patient	**1804**	**88%**	**84%**	**75%**	**65%**	**56%**				**Patient**	**1499**	**90%**	**86%**	**76%**	**64%**
Hepatic adenoma	38	2%	0.03%	Graft	38	65%	47%	40%	40%	40%	30	2%	0.03%	Graft	30	70%	44%	44%	
				Patient	38	71%	55%	55%	55%	55%				Patient	30	73%	52%	52%	
Adenomatosis	51	3%	0.04%	Graft	49	81%	81%	81%	81%		45	3%	0.05%	Graft	43	81%	81%	81%	
				Patient	49	87%	87%	87%	87%					Patient	43	88%	88%	88%	
Hemangioma	71	4%	0.1%	Graft	71	75%	69%	64%	64%	64%	45	3%	0.05%	Graft	45	73%	64%	64%	64%
				Patient	71	80%	77%	71%	71%	71%				Patient	45	75%	69%	69%	69%
Focal nodular hyperplasia	12	1%	0.01%	Graft	12	75%	64%	21%			10	1%	0.01%	Graft	10	80%	80%	27%	
				Patient	12	92%	92%	32%						Patient	10	90%	90%	45%	
Polycystic disease	1493	82%	1%	Graft	1478	87%	82%	73%	62%	52%	1293	85%	1%	Graft	1280	88%	83%	73%	61%
				Patient	1478	90%	86%	78%	67%	54%				Patient	1280	91%	87%	79%	65%
Nodular regenerative hyperplasia	25	1%	0.02%	Graft	25	88%	71%	71%	36%	36%	17	1%	0.02%	Graft	17	100%	83%	83%	

				Patient	25	88%	71%	71%	36%	36%				Patient	17	100%	83%	83%	
Other benign tumors: specify	134	7%	0.1%	Graft	131	79%	71%	60%	49%	44%	76	5%	0.1%	Graft	74	82%	73%	56%	56%
				Patient	131	83%	76%	66%	54%	49%				Patient	74	86%	79%	62%	62%
Parasitic disease	**101**		**0.1%**	**Graft**	**101**	**77%**	**69%**	**58%**	**40%**	**20%**	**71**		**0.1%**	**Graft**	**71**	**81%**	**70%**	**70%**	
				Patient	**101**	**80%**	**72%**	**61%**	**45%**	**27%**				**Patient**	**71**	**84%**	**73%**	**73%**	
Schistosomia (Bilharzia)	2	2%	0.002%	Graft	2	50%	50%	50%	50%		1	1%	0.001%	Graft					
				Patient	2	50%	50%	50%	50%					Patient					
Alveolar echinococcosis	58	57%	0.05%	Graft	58	88%	80%	66%	66%		49	69%	0.1%	Graft	49	90%	78%	78%	
				Patient	58	90%	81%	67%	67%					Patient	49	92%	80%	80%	
Cystic hydatidosis	11	11%	0.01%	Graft	11	72%	57%	57%	29%		8	11%	0.01%	Graft	8	74%	49%		
				Patient	11	71%	57%	57%	28%					Patient	8	74%	49%		
Other parasitic disease: specify	30	30%	0.02%	Graft	30	60%	56%	44%	22%	22%	13	18%	0.01%	Graft	13	60%	60%	60%	
				Patient	30	68%	64%	52%	33%	33%				Patient	13	69%	69%	69%	
Other liver disease	**2380**		**2%**	**Graft**	**2325**	**73%**	**64%**	**56%**	**50%**	**42%**	**1302**		**1%**	**Graft**	**1264**	**75%**	**67%**	**59%**	**43%**
				Patient	**2318**	**77%**	**69%**	**61%**	**55%**	**47%**				**Patient**	**1263**	**80%**	**72%**	**64%**	**49%**
TPN-induced cholestasis	11	0.5%	0.01%	Graft	11	71%	54%				10	1%	0.01%	Graft	10	68%	46%		
				Patient	11	71%	54%							Patient	10	68%	46%		
Hepatopulmonary syndrome	19	1%	0.01%	Graft	18	78%	78%				19	1%	0.02%	Graft	18	78%	78%		
				Patient	18	78%	78%							Patient	18	78%	78%		
Other liver diseases. non-specified	2350	99%	2%	Graft	2296	73%	64%	56%	50%	42%	1273	98%	1%	Graft	1233	75%	67%	59%	43%
				Patient	2289	77%	69%	61%	55%	47%				Patient	1232	80%	72%	64%	49%
Total	**127851**		**100%**								**91183**		**100%**						

Table 1